ENERGY DRINKS AND CAFFEINE: THE SCIENCE BEHIND THE BILLION-DOLLAR INDUSTRY

by

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ABSTRACT

ERIC VILLARREAL: Energy Drinks And Caffeine: The Science Behind The Billion-Dollar Industry

(Under the direction of Susan Pedigo)

Ask any college student how he or she gets through long study sessions, all-nighters, and the always grueling finals week and he or she will most likely reference some caffeine-containing beverage as the antidote, with energy drinks becoming an ever increasing option. The effects, both physiological and psychological, of the ingredients in energy drinks (caffeine and, to a lesser degree, glucose) dictate their usefulness to consumers. A review of the available research literature from http://scholar.google.com using the following keywords: "caffeine," "energy drink," "Red Bull," "caffeinated beverage," "caffeine drink," "energy drink industry," "energy drink company," and "glucose" yielded the references that have been aggregated, synthesized, and summarized in this thesis. Caffeine's ability to improve one's subjective mood, reaction time, memory, and attention has been scientifically verified by the available research literature; in essence, then, caffeine is a legal, low-grade stimulant. The ubiquity of caffeine in everyday life has made its consumption a part of everyday life and a normal means of self-medication. This ubiquity in today's society has also been promoted by the lax regulatory structure regarding the compound – a regulatory structure that has allowed EDs manufacturers to include five times more caffeine in their products than in a can of Coca-Cola. EDs manufacturers have embraced caffeine's stimulatory effects in such an atmosphere of lax regulation and high demand produced by environmental and societal factors to produce high-caffeine, high-sugar products uniquely suited to their target demographic – twenty year olds. However, they also dictate the negative side effects that can harm consumer health over the short or long-term.

TABLE OF CONTENTS

List of Abbreviations

2CRT	Two Choice Reaction Time
ATP	Adenosine Triphosphate
BP	Blood Pressure
CAF	Caffeine supplement
cAMP	Cyclic Adenosine Monophosphate
CNS	Central Nervous System
DV	Daily Value
ED	Energy Drink
EPSP	Excitatory Post-Synaptic Potential
FDA	Food and Drug Administration
GI	Gastrointestinal
GRAS	Generally Recognized As Safe
HR	Heart Rate
POMS	Profile of Mood States
SRT	Simple Reaction Time
RVIP	Rapid Visual Information Processing
VAS	Visual Analogue Scale

Chapter 1: The Energy Drink Industry

Since 1987, a growing phenomenon has swept the world. It started in Austria and quickly expanded to include other European countries and the United States. This phenomenon, this substance, allows consumers to stay up later, focus longer, and push through that “2:30 feeling”. It exhibits all the stimulant effects of amphetamine (at a significantly less intense and safer level), yet seems to be as common as coffee. And that is because it is very much like coffee; it is an energy drink. With the invention of Red Bull in Austria in 1987, energy drinks have quickly established a foothold in grocery stores and gas stations across America (Ishak, Ugochukwu, Bagot, Khalili, & Zaky, 2012). In our go-go-go society, these stimulants in a can allow us to do the impossible – replace sleep with a beverage and then go about our business. Like coffee, energy drinks (EDs) allow individuals to ignore their own fatigue or tiredness and keep on going – a seemingly wonderful invention if you are that individual, but at what cost? Because everything in this world seems to have a cost and, surely, the price on the can is not the only price you pay when consuming such useful products. And how exactly does an ED work? What is the active ingredient in that ED that you consume on your way to a late-night study session or early morning work meeting? It is these questions, and so many more, that consumers need to ask themselves as they ingest their favorite ED.

Growth of an Industry

Though relatively young (Red Bull was not introduced in the United States until 1997), the ED industry has quickly expanded and become a multibillion-dollar industry in the process (Ishak et al., 2012). In the five years between 1998 and 2003, U.S. ED sales increased approximately 465%, demonstrating spectacular growth in only their first six years on the market (Clauson, Shields, McQueen, & Persad, 2008) in the four-year period from 2003-2007, the ED industry saw 400% growth, proof of their ability to maintain strong sales and a viable place in the U.S. beverage industry (Howard & Marczinski, 2010). From 2008-2012, the last years of available sales data, this industry grew a relatively low 60% (Beyerstein, 2013), indicating possible saturation of the ED market. In 2006 alone, 906 million gallons of EDs were sold, producing some $5 billion in sales (Clauson et al., 2008; Reissig, Strain, & Griffiths, 2009), while in 2009, they produced an estimated $4.6 billion (Berger, Fendrich, Chen, Arria, & Cisler, 2011); it was also reported that 354.5 million gallons of EDs were sold in the United States in 2009 (Somogyi, 2009). The year 2012 showed a 16% increase in sales from the previous year and an evaluation of the ED industry at $12.5 billion (Markey, Durbin, & Blumenthal, 2013). That is an increase of approximately $8 billion in the three years since 2009. All of these statistics are evidence of the constant growth experienced by ED companies and their successful campaigns to market these drinks, though there does appear to be a slowing down of their growth in recent years; this could be due to saturation of the market and/or increasing awareness of the health implications of ED consumption.

Energy Drinks on the Market

Today, common EDs include Red Bull, Monster Energy, Rockstar, NOS, AMP, Full Throttle, and 5-hour ENERGY, with the first three being considered the leading ED brands and the last one the leading energy shot (Somogyi, 2009). Red Bull and Monster, alone, accounted for 80% of all ED sales in the fiscal year 2013 (Ferdman, 2014). In the U.S., these leading brands showed annual growth in excess of 50% from 2001 to 2006 but those numbers have since declined to 9% in 2008 and only 0.2% in 2009 (Beyerstein, 2013). Globally, however, their growth has been even more explosive. – 620% since 1999 (Ferdman, 2014). Currently, Red Bull makes up 42% of the ED market, followed by Monster with 37% and Rockstar with 11%. In the energy shot market, characterized by energy drinks of just a few fluid ounces, 5-hour ENERGY dominates with ownership of 90% of the market (Beyerstein, 2013). Improvements in ingredient disclosures due to FDA prompting has allowed consumers to see first-hand what is contained within most EDs (Markey et al., 2013).

Red Bull

The first product in a new beverage category, Red Bull laid the foundation for the entire ED drink industry both with its product and its marketing. “Functional drinks” from the Far East were what inspired Dietrich Mateschitz to found Red Bull, and on April 1, 1987, the first can of Red Bull was sold in Austria (Bull, 2014b). According to its website, over 35 billion cans of Red Bull have been consumed in over 165 countries since then (Bull, 2014c). Furthermore, in 2012 alone, Red Bull sold over 5.2 billion cans, an increase of 12.8% over the previous year. This resulted in 15.9% growth for a company as a whole, resulting in Red Bull’s best sales figures to date. These strong numbers were due in large part to an increase in sales of 52% and 51% in South Africa and Japan, respectively. The United States saw sales increases of 17% (Bull, 2014b). The homepage of the Red Bull website touts its product with the following statement:

> In 1987, Red Bull not only launched a completely new product, it created a whole new product category — Energy Drinks. (Bull, 2014a)

Thus, Red Bull quite literally created a whole new drink genre. No longer would coffee suffice the needs of sleep-deprived, hard working Americans. Instead, many have turned to these high-energy, high-caffeine beverages to satisfy their needs. The actual beverage, produced in Santa Monica, CA, contains the following: 110 calories, carbonated water, 21.5 g sucrose, 5.25 g glucose, citric acid, 1,000 mg taurine, 600 mg glucuronolactone, 80 mg caffeine, 50 mg inositol, vitamins (niacin, pantothenic acid, B6, B12), as well as riboflavin (a component of the electron carrier, FAD) (Alford, Cox, & Wescott, 2001). Additionally, Red Bull also comes in a sugar-free version. Interestingly, of the popular EDs currently on the market, Red Bull is most commonly bought in its 8oz. form, with half the caffeine content of most other EDs. Thus, this King of the EDs actually contains less caffeine than most of its other competitors, though the ratio of caffeine/ounce is still the same as drinks such as NOS and Monster – those EDs contain twice the caffeine in a can that is twice the size as Redbull's. Red Bull's ascent to the top can be ascribed to its status as the first on the market, as while as the its excellent marketing and sponsorship campaigns.

Monster Energy

Produced by Monster Energy Company of Corona, CA, Monster Energy is another popular ED sold today, as exemplified by its inclusion in vending machines across the Ole Miss campus. As indicated on the can, this drink consists of the "Monster Energy Blend," including glucose, taurine, panax ginseng extract, L-carnitine, caffeine, glucuronolactone, inositol, guarana extract, and maltodextrin. A 16 oz. can of Monster contains a listed 210 calories, 54 g of sugar in the form of glucose, and 160 mg of caffeine, as well as 200% DV of vitamins B2 (riboflavin), B3 (niacin), B6 (pyridoxine hydrochloride), and B12 (cyanocobalamin). The listed caffeine content is in line with an experimentally determined content of 184 mg by Consumer Reports (Reports, 2012). Like Red Bull, Monster's popularity has grown thanks, in part, to excellent marketing campaigns, such as its current one with Call of Duty: Ghosts, a popular video game. By connecting itself with other popular brands, Monster has increased its visibility with consumers.

NOS

Produced by Energy Brands Inc., a subsidiary of Coca Cola, this ED contains 210 calories, 160 mg caffeine, 53 g of sugar (high fructose corn syrup) in 54 g of carbohydrates, as well as carbonated water, citric acid, taurine, L-theanine, guarana and vitamins B6 and B12 all in a 16 oz. can. The makers of NOS market the combination of caffeine, guarana, B12, B6, L-theanine, and taurine as "CMPLX6" on the can. While cans of NOS today list caffeine content at 160 mg, it appears that as recently as an April 2013 Congressional Report those same cans had 260 mg of caffeine (Markey et al., 2013). A Consumer Reports study on caffeine levels in EDs completed in December 2012 found that NOS contained 224 mg of caffeine (Reports, 2012). The reason for the discrepancies between these three numbers is unknown, though it does appear that the lower caffeine levels found in cans of NOS today might be due to recent Congressional pressure and public support for the change. Nevertheless, NOS remains a popular choice among ED users and can also be found in vending machines across the Ole Miss campus.

Rockstar

Rockstar, manufactured by Rockstar Inc. out of Las Vegas, NV, is another popular ED on the market today. Each 16 oz. can of Rockstar contains, according to its "Nutrition Facts" label, 280 calories, 80 mg of sodium, 62 g of sugar (sucrose and glucose), as well as 200% of the daily value of vitamins B6 and B12 and niacin and 400% of the daily value of riboflavin (a key component of FAD, a biological electron acceptor with an important role in metabolism). Additional ingredients in Rockstar include 2,000 mg of taurine, 160 mg of caffeine, guarana seed extract (which also contains caffeine), 50 mg of L-carnitine, and 50 mg of inositol. Rockstar also contains *panax ginseng* root extract and milk thistle extract.

5-hour ENERGY

The most popular energy shot on the market (Beyerstein, 2013), 5-hour ENERGY makes a name for itself by promoting its sugar-free flavors and lack of sugar crash after ingestion. The supplement facts on each can list 150% daily value (DV) of niacin, 2,000% DV of vitamin B6, 8,333% DV of vitamin B12, and a 1,870 mg energy blend consisting of taurine, glucuronolactone, and caffeine, among other ingredients. Additionally, Markey et al. (2013) claim that 5-hour ENERGY contains methylated xanthine, a synthetic stimulant very similar to caffeine as it only lacks two of the three methyl groups found on the caffeine xanthine ring. Thus, this particular energy shot contains not only some of the highest caffeine levels found on the market, but also an additional stimulant most consumers are not aware of. While it is not listed under the supplement facts on the 5-hour ENERGY website or cans, its inclusion in the drink is possible because, as a dietary supplement, 5-hour ENERGY is not required to disclose all of its ingredients (Markey et al., 2013).

Table 1: Comparison of ED ingredients (Reports, 2012)

ED	Container Size (oz.)	Calories	Caffeine (mg)	Sugar (g)	Taurine (mg)	Vitamin B6 (%DV)	Vitamin B12 (%DV)
Red Bull	8	110	**80**	27	1,000	250	80
Monster Energy	16	210	**160**	54	UN	200	200
NOS	16	210	**160**	53	UN	200	200
Rockstar	16	280	**160**	62	2,000	200	200
Full Throttle	16	230	**160**	58	?	200	200
5-hour ENERGY	1.9	4	**215**	0	UN	2000	8333

UN = Present but in an unknown amount
-- = Not present
? = Unknown

Consumer Numbers and Motivations

As of 2008, there were an estimated 34.5 million ED consumers in the United States alone, most of who fall into the younger age groups (Berger et al., 2011). In a community survey, 31.4% of respondents indicated that they have consumed EDs in their lifetime, while 26.3% had consumed one or more in the past year (Berger et al., 2011). These statistics show that EDs have become increasingly prevalent in today's society but tell nothing of why this is the case. Why is it that 1 in 4 Americans consumed at least one ED in the last year (25% incidence rate) while nearly 1 in 3 have consumed an ED in their lifetime (33% prevalence rate)? The answer lies partly in consumer motivations. A study published in 2007 examined the motivations behind ED consumption in a sample of college students. In the study, 51% of respondents reported consuming more than one ED in an average month of a school semester (Malinauskas, Aeby, Overton, Carpenter-Aeby, & Barber-Heidal, 2007). Among these ED users, 67% used them to prevent falling asleep; 65% to increase their energy levels; 54% as a mixer with alcohol; and 50% while studying or completing a major project (Malinauskas et al., 2007). These were the most common reasons college students reported consuming EDs; thus, approximately two-thirds of college students who do drink EDs drink them to compensate for poor sleep or energy, which is a function of sleep. These consumer motivations are uniquely satisfied by the effects of the ingredients in each ED – specifically, the effects of caffeine. Thus, ED manufacturers have found their niche in which they answer these consumer demands with a drink containing a substance whose effects are the very effects consumers are looking for. To understand how EDs work, then, one must first examine the ingredients within an ED.

Chapter 2: Energy Drink Constituents

Thanks to recent improvements in the disclosure of energy drink (ED) ingredients on “Nutrition Facts” labels, one can see that common ingredients in today’s ED include caffeine; sugars such as glucose, sucrose, ribose, and high fructose corn syrup; guarana, taurine, ginseng, niacin (Vitamin B3), glucuronolactone, inositol, and carnitine, as well as additional vitamins. Research has shown that caffeine, by and large, is the primary ingredient responsible for the physiological and cognitive effects of ED consumption. This is due to both the high levels of caffeine and the low levels of the other ingredients found in these drinks (Clauson et al., 2008; Scholey & Kennedy, 2004). Indeed, multiple studies have shown that the caffeine levels present in EDs exceed the minimum level needed to elicit both physiological and psychological change, while the levels of other ingredients, except perhaps those of glucose, are well below their respective therapeutic doses (Clauson et al., 2008; Haskell, Kennedy, Wesnes, & Scholey, 2005; Kennedy & Scholey, 2004; Smit, Cotton, Hughes, & Rogers, 2004). One such study found that the levels of herbal extracts found in EDs is 1-3% of their respective psychoactive doses and concluded that these extracts exist for flavoring purposes only and do not contribute to the cognitive effects produced by ED consumption (Scholey & Kennedy, 2004).

Caffeine

The main active ingredient in energy drinks, caffeine is also found in other common beverages such as soft drinks, tea, and coffee; the only difference is that caffeine is often found in much higher quantities in energy drinks than in these other beverages. Red Bull, for instance, contains 80 mg of caffeine per 8 ounce can, while NOS, another popular ED, contains 160 mg of caffeine per 16 ounce can. In contrast, the FDA generally recognizes as safe (GRAS) a caffeine concentration of 71 mg per 12 fluid oz in soft drinks (Markey et al., 2013), and the average caffeine concentration of most soft drinks is 34 mg per 12 oz. can (Ishak et al., 2012). Because of its prolific use in so many different beverages, caffeine has been declared the most widely consumed psychoactive compound in the world today (Babu, Church, & Lewander, 2008; Carrillo & Benitez, 2000; Childs & de Wit, 2008). This is an apt description, due to both its wide availability and effects on the central nervous system. A recent FDA report revealed that Americans, on average, consume about 300 milligrams of caffeine each day (Somogyi, 2009). Because of its importance, more discussion will be spent on this ingredient than any other. Natural sources of caffeine include guarana, kola nut, tea, yerba mate, and cocoa (Babu et al., 2008; Ishak et al., 2012). So, yes, that does mean caffeine is found in chocolate. To understand caffeine's effects on the body, one must first examine the chemical structure of caffeine, as its microscopic structure and effects produce its macroscopic cognitive and physiological effects.

Structure and Absorption

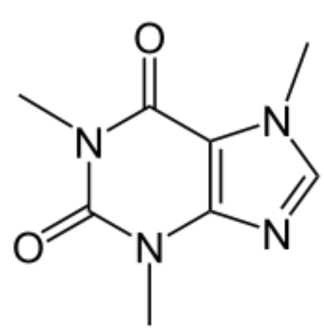


Figure 1: Caffeine

Caffeine’s IUPAC name is 1,3,7-trimethylxanthine, denoting the presence of three methyl groups around a xanthine cyclic structure (see Figure 1 above). It is a bitter white crystalline alkaloid that is recognized by the FDA as a “Multiple Purpose Generally Recognized as Safe Food Substance,” meaning it is allowed for use in both food and beverages with little to no restrictions (Somogyi, 2009). Its chemical structure is important for many reasons, the first of which is its ability to diffuse through plasma membranes within the body, allowing for complete and fast absorption upon ingestion. Caffeine can do this, as its hydrophobicity is enough to allow it to pass through the hydrophobic lipid bilayer of cell membranes (Carrillo & Benitez, 2000). Thus, when caffeine is orally ingested, it passes into the stomach and then to the GI tract, where it is quickly absorbed into the bloodstream and distributed throughout the body, passing through the blood-brain barrier and into the brain (Babu et al., 2008; Carrillo & Benitez, 2000). Within the bloodstream, due to its hydrophobic nature, caffeine is estimated to be 10-35% protein bound to allow for transport through the aqueous environment of the blood (Babu et al., 2008). Even though it is absorbed from the small intestine and passes through the liver via the hepatic portal vein on its way to the rest of the body, little first-pass effect is reported, allowing for maximum (i.e., 100%) bioavailability within the body (Babu et al., 2008; Carrillo & Benitez, 2000). Upon consumption, peak caffeine plasma levels are reached within thirty to sixty minutes, depending on a number of factors affecting metabolism and digestion, as confirmed by multiple sources (Alford et al., 2001; Astrup et al., 1990; Ishak et al., 2012; Kennedy & Scholey, 2004; Warburton, Bersellini, & Sweeney, 2001). Research by Astrup et al. (1990) confirms that peak caffeine concentration is reached at approximately 30 minutes after ingestion (see Figure

2 below, each data point represents a 30 minute interval starting at 30 minutes pre-ingestion). Figure 2 also demonstrates the ability of higher caffeine doses to elicit a higher blood caffeine concentration, both immediately and over time. Caffeine's complete and rapid absorption is instrumental in its usefulness to humans, as its effects are thus elicited relatively fast for an oral administration substance. Thus, an individual can consume an ED and begin to experience its cognitive and physiological effects within half an hour, allowing for quick relief of fatigue and a much-needed boost of energy.

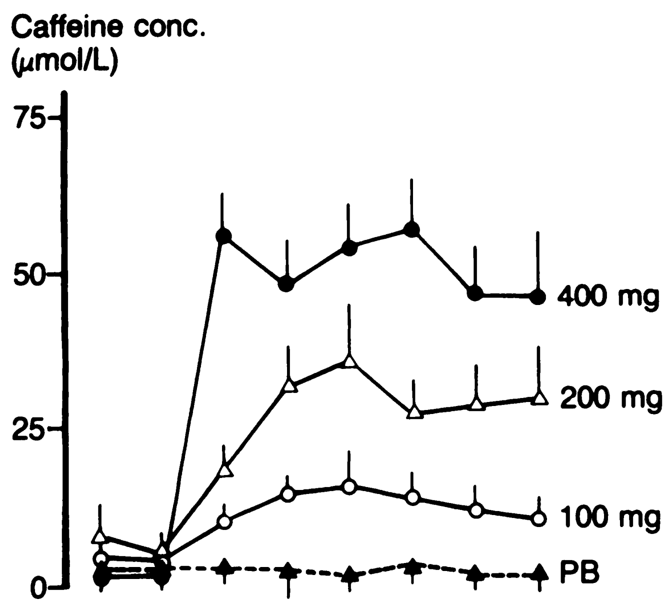


Figure 2: Caffeine Concentration Over Time (Astrup et al., 1990)

Mechanisms of Action

Once within the central nervous system (CNS), caffeine's mechanisms of action consist of adenosine receptor antagonism, phosphodiesterase inhibition, and calcium mobilization within the muscles (Carrillo & Benitez, 2000; Clauson et al., 2008; Ishak et al., 2012). Of the three reported mechanisms of action, adenosine receptor antagonism is the most relevant to caffeine's stimulant effects, while the latter two are implicated in its toxic effects (Carrillo & Benitez, 2000; Nehlig & Boyet, 2000). In regards to adenosine receptor antagonism, caffeine acts as a competitive antagonist on adenosine A_1 and A_{2A} receptors, blocking them and thereby preventing the binding of adenosine (Carrillo & Benitez, 2000; Ishak et al., 2012; Smit et al., 2004). Its role as a competitive antagonist allows for the possibility the caffeine would not work (that is, it would not exerts its effects) when adenosine levels are significantly high. In such an instance, adenosine would preferentially bind to adenosine receptors and caffeine would be unable to compete for binding sites. Caffeine preferentially binds to A_{2A} receptors at low doses. These adenosine receptors co-localize with dopamine D2 receptors in the striatum, establishing an A_{2A}-D2 pathway that explains most of its effects (Nehlig & Boyet, 2000). When caffeine binds to these adenosine receptors, its antagonistic action blocks the inhibitory effects of adenosine on these dopaminergic neurons, allowing for increased dopamine secretion. At higher doses, caffeine begins to bind to the other adenosine receptor, A_1. This receptor co-localizes with dopamine D1 receptors also in the striatum and caffeine's antagonistic actions go into effect (Nehlig & Boyet, 2000). The blockade of adenosine receptors by caffeine results in the inhibition of adenosine's actions on the CNS, specifically the inhibition of dopamine release, leading to a subsequent increase in neurotransmitter levels, especially levels of dopamine (Smit et al., 2004). Any increase in dopamine levels would seem to have a positive, reinforcing effect on caffeine administration, as dopaminergic pathways within the brain serve as the brain's reward center and are implicated in many drugs of abuse and their addictive natures. Research has shown that while caffeine does activate these pathways, it only does so at very high doses (<10 mg/kg) injected intravenously (Nehlig & Boyet, 2000). Specifically, such a dose has been shown to activate dopamine release in the shell of the nucleus accumbens, the key brain structure in "emotions, motivation, and reward functions"; lower doses more in line with everyday human consumption do not activate this structure and so fail to activate the brain's reward pathways, even if they have moderate reinforcing effects (Nehlig & Boyet, 2000). Nevertheless, it is important to understand that the majority of caffeine's effects on the body are a result of its ability to inhibit the effects of adenosine agonists and its ability to promote dopamine excretion and sympathetic nervous system activation through its adenosine antagonism.

Metabolism and Elimination

Caffeine metabolism occurs within the liver, where caffeine molecules are metabolized by cytochrome P450 1A2 (CYP 1A2) through three main demethylation reactions (Carrillo & Benitez, 2000). The CYP 1A2 isozyme is responsible for more than 95% of caffeine metabolism, and removal of the methyl group at carbon #3 is the main demethylation reaction, with demethylation at carbon #1 and carbon #7 accounting for the second and third most common metabolic reactions, respectively (Carrillo & Benitez, 2000). The variability in the metabolic rate of CYP 1A2 among different individuals accounts for the wide range in the estimated caffeine half-life, ranging from 3-6 hours depending on the individual (Alford et al., 2001; Carrillo & Benitez, 2000). Furthermore, Carrillo & Benitez (2000) showed that the elimination half-life of caffeine can be twice as long in non-consumers compared to caffeine consumers (7.5 hours and 4 hours, respectively) This would seem to indicate increased caffeine metabolism due to up-regulation of CYP 1A2 in habitual caffeine consumers, an indication of possible caffeine tolerance; it would also mean that non-consumers are more vulnerable to high caffeine doses, as their body cannot clear the drug as quickly.

Effects on the Body

Caffeine, through its mechanisms of action, has many effects on the body, all of which should occur after ED consumption. Caffeine's effects on heart rate are mediated by two separate and opposite pathways: one involves the antagonism of adenosine receptors at sympathetic neurons, resulting in increased norepinephrine release and a subsequent increase in heart rate, while the other involves the activation of medullary vagal nuclei, which leads to decreased heart rate (Scholey & Kennedy, 2004). Its effects on the heart are thus varied, as some studies reported decreased or unaffected heart rate (Childs & de Wit, 2008; Scholey & Kennedy, 2004) while others reported an increase in heart rate (Alford et al., 2001; Clauson et al., 2008) and still others reported a diphasic response in which both increased and decreased heart rate were seen (Astrup et al., 1990). In a 2004 study, a drink containing 37.5 g of glucose (but no caffeine) was shown to significantly increase heart rate, while another containing 75 mg of caffeine (but no glucose) significantly reduced heart rate (Scholey & Kennedy, 2004). These findings are especially interesting, as EDs contain both caffeine and sugar; perhaps the inclusion of both ingredients results in a beverage with no overall effect on heart rate. It is important to note that Red Bull was the caffeine-containing beverage in Alford et al.'s (2001) research which showed an increase in heart rate, so the effects of its other ingredients, including glucose, might have played a role in the study outcome, especially since glucose has been shown to significantly increase heart rate in and of itself (Scholey & Kennedy, 2004). Research by Astrup et al. (1990) revealed the presence the presence of the “diphasic response” in which caffeine ingestion leads, first, to a decrease in heart rate between 30-90 minutes after consumption followed by a subsequent increase at 90-180 minutes (Astrup et al., 1990). It would appear, then, that activation of the medullary vagal nuclei is followed by adenosine antagonism leading to greater norepinephrine release. Caffeine has also been reported to increase the strength of cardiac muscle contraction (Clauson et al., 2008) as well as systolic and diastolic blood pressure (Childs & de Wit, 2008; Clauson et al., 2008) body vitals that are connected as the strength of cardiac muscle contraction influences the systolic blood pressure, which is the blood pressure at the time of heart chamber contraction. The same study that found caffeine consumption of 200 mg significantly increased systolic blood pressure did, however, find no significant effect on diastolic blood pressure (Childs & de Wit, 2008). Another study examining the effects of 400 mg of caffeine found that it significantly increased both systolic and diastolic blood pressure, indicating a measure of dose-dependency in caffeine’s effects on blood pressure (Astrup et al., 1990). Additionally, Glade (2010) found that caffeine doses in excess of 300 mg tended to increase both systolic and diastolic blood pressure over multiple studies. Thus, while studies examining the effects of caffeine doses below 80 mg (the amount of caffeine found in your average 8oz. ED) found no significant effects on BP, studies examining caffeine doses in excess of approximately 300 mg (which would constitute 2-3 EDs) found significant, though temporary, increases in blood pressure. These results indicate that the caffeine doses found in most EDs will have no effect on one’s blood pressure, but that the rapid consumption of multiple cans or EDs with caffeine in excess of 300 mg would increase blood pressure. These temporary increases, however, do not appear to translate into hypertension, as an analysis of data from the Nurses' Health Studies I and II shows no association between chronic caffeine consumption and hypertension and the FDA itself has concluded that chronic caffeine consumption has no effect on blood pressure after a mere two weeks (Glade, 2010).

Caffeine's effects on the body also extend well beyond the cardiopulmonary system; indeed, caffeine has been reported to have effects on metabolism as a whole, including an increase in the metabolic rates of lipolysis, glycogenolysis, and gluconeogenesis (Astrup et al., 1990; Kennedy & Scholey, 2004; Scholey & Kennedy, 2004; Smit et al., 2004). Increases in these metabolic processes lead to increased energy charge in the form of ATP production through glucose oxidation. Indeed, a study performed in 1990, seven years before the introduction of Red Bull to the American market, showed that 100, 200, and 400 mg doses of caffeine all significantly increased the body's "integrated thermogenic response" compared to a placebo in terms of kcal/h; the 400 mg dose produced the greatest increase, to the tune of 32 kcal/h over the placebo (Astrup et al.). The researchers themselves concluded that this increase was due to an increase in both carbohydrate and lipid oxidation and might suggest an increase in the Cori cycle's transformation of lactate to glucose in the liver and glucose to lactate in anaerobic muscle tissues (Astrup et al., 1990). These effects mean that caffeine, overall, increases resting metabolic rate (Glade, 2010). Caffeine has also been shown to be a vasodilator, increasing the diameter of blood vessels (Smit et al., 2004), and a broncodilator, increasing the diameter of the bronchioles of the lung (Astrup et al., 1990). Its actions as a vasodilator might be behind the headaches commonly experienced during caffeine withdrawal. Decreased blood flow, due to vasoconstriction in the absence of caffeine, in brain blood vessels previously dilated by the presence of caffeine might cause such withdrawal headaches. Within the brain, caffeine reportedly increases catecholamine release and triggers CNS activation through increased cAMP concentration in postsynaptic cells (Glade, 2010; Smit et al., 2004). Concentration enhancement of this common second messenger “may increase the strength of transmitted signals” by increasing the strength of EPSPs (excitatory post-synaptic potentials) facilitated by cAMP cascades (Glade, 2010). Caffeine’s effects also extend to the renal system, where it acts as a diuretic with an estimated water loss of 1.17 mL/mg caffeine (Carrillo & Benitez, 2000; Clauson et al., 2008). Water and electrolyte loss due to caffeine ingestion makes EDs an inappropriate pre or post-workout beverage due to their enhancement of dehydration.

Table 2: Summary of Caffeine’s Main Effects on Human Organs

Organ	Effect
Liver	Increased lipolysis, glycogenolysis, gluconeogenesis, Cori cycle activation → increased basal metabolic rate
Heart	Diphasic response consisting of both increased and decreased HR, increased BP (though only temporarily)
Kidneys	Diuretic action resulting in increased water and electrolyte loss
Brain	Adenosine receptor antagonism, vasodilation, increased catecholamine and cAMP release, CNS activation
Lungs	Broncodilation

Caffeine Withdrawal

The symptoms of caffeine withdrawal, as described by the literature, include headache, drowsiness, fatigue, decreased energy, concentration, mood, impaired cognition, insomnia, and restlessness (Carrillo & Benitez, 2000; Haskell et al., 2005). These symptoms typically begin within 12-24 hours of caffeine cessation, reach their apex of severity within 1-2 days, and last as long as a week (Babu et al., 2008). It has been noted that caffeine withdrawal can occur even after the administration of low doses of caffeine for just a few days, implying that the regular consumption of EDs followed by a complete and sudden abstinence would also elicit these symptoms (Babu et al., 2008). Withdrawal from a psychiatric compound is typically followed first by tolerance and dependence to said compound, and caffeine does seem to demonstrate tolerance, dependence, and withdrawal, all key features of any drug of abuse (Carrillo & Benitez, 2000). It has been reported that caffeine tolerance can occur within a few days of regular caffeine consumption, which would line up nicely with the reports of the caffeine withdrawal timeline (Carrillo & Benitez, 2000).

Caffeine dependence, a sign of possible caffeine withdrawal according to Berger et al. (2011), has also been reported in the scientific literature. A study published in the *Journal of the American Medical Association* found that 16% of caffeine-consuming subjects were found to have caffeine dependence as defined by the DSM-IV, while 94% of subjects underwent withdrawal after caffeine abstinence (Strain, Mumford, Silverman, & Griffiths, 1994). The relatively low rate of participants with diagnosable caffeine dependence is not surprising, as neurological research has shown that caffeine has a relatively low ability to elicit addiction, as it does not activate the shell of the nucleus accumbens, the key brain structure in addiction (Nehlig & Boyet, 2000). The high rate of participants who underwent caffeine withdrawal is not surprising, as common sense and everyday observation tells us that most chronic caffeine consumers simply are not "morning people" before their first cup of coffee or that first ED.

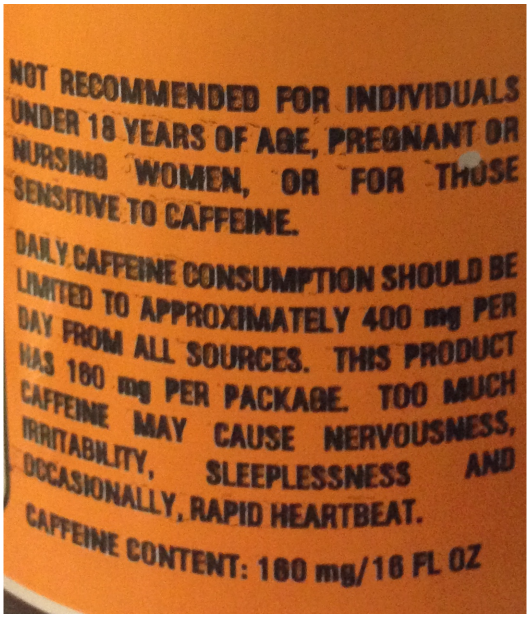
These withdrawal symptoms are obviously negative in nature and thus seem to enhance the reinforcing effects of caffeine consumption (Carrillo & Benitez, 2000). Because of this, some researchers have hypothesized that repeated caffeine consumption serves to alleviate or reverse the negative withdrawal symptoms brought about by caffeine abstinence instead of providing positive benefits above and beyond mere withdrawal symptoms (Babu et al., 2008; Smit et al., 2004). That is, individuals regularly consume caffeine not only because it provides them with any net benefits but also because it mitigates the negative symptoms of overnight withdrawal. Psychological speaking, this is a common example of negative reinforcement – the phenomenon in which a behavior is promoted because of its ability to reduce or mitigate a negative event. Through negative reinforcement, an important part of operant conditioning, ED consumption can be promoted as a behavior because of its ability to mitigate the negative effects of caffeine withdrawal. Thus, caffeine consumption in the form of EDs is promoted through both positive and negative reinforcement.

However, the caffeine withdrawal alleviation model, as it is called, has been disproved in other studies that have shown that caffeine does, in fact, provide positive effects or that there exist no baseline differences between caffeine-deprived consumer and non-consumer groups in experimental studies (Alford et al., 2001; Haskell et al., 2005; Howard & Marczinski, 2010). In another study, the consumption of Red Bull (of which caffeine is the primary ingredient) produced positive cognitive effects in participants who could not have been in caffeine withdrawal due to unrestricted caffeine consumption before testing (Warburton et al., 2001). This is an important experimental condition in the quest to determine if caffeine withdrawal is the main source of caffeine's effects, as most previous caffeine-related experiments had been performed on subjects deprived of caffeine overnight, if not longer, allowing for the possibility of withdrawal alleviation effects. Another study showed that the effects produced by caffeine did not vary even with the level of habitual caffeine consumption in those who regularly consume the ingredient; this same study did, however find a correlation between average caffeine consumption and decreased vigor at 3 a.m. due to withdrawal (Childs & de Wit, 2008). Childs and de Wit (2008) posited that this might reflect the effects of caffeine withdrawal in individuals with high regular consumption patterns.

Thus, the body of research on caffeine withdrawal does verify its existence but also demonstrates caffeine's efficacy above and beyond simple alleviation of its withdrawal symptoms. The most recent development in the debate over caffeine withdrawal is its inclusion in the DSM-V under the category of "Caffeine-Related Disorders" (Peckham, 2013). Indeed, the newest edition of the *Diagnostic and Statistical Manual of Mental Disorders*, the American Psychiatric Association's official handbook to diagnosing mental disorders, has now given legitimacy to this withdrawal syndrome and verified that all of the headaches and fatigue you have ever felt hours after consuming that massive cup of Starbucks coffee or 16oz ED were a consequence of your body's withdrawal from the substance. Nevertheless, the presence of these withdrawal symptoms does seem to reinforce chronic caffeine consumption, as evidenced by hordes of "regulars" at Starbucks lines all across America and the masses of chronic Red Bull consumers who live and breathe by it ("it" being the drink). Regular caffeine consumption, for them, is a cycle of withdrawal and alleviation with withdrawal occurring every morning when they wake up and alleviation coming with that first cup of coffee or first downed ED. It is this cycle that keeps the consumer coming back for more, creating habitual consumers who thereby feed the ED industry and allow it to grow.

Adverse Effects

The adverse effects of caffeine are well documented and typically occur after excessive caffeine consumption or its use by a caffeine-sensitive individual; examples of these adverse effects include headaches, nausea, heart palpitations, seizures, tachycardia, and rhabdomyolysis (Babu et al., 2008). Malinauskas et al. (2007) reported that 22% and 19% of ED users surveyed reported headaches and heart palpitations, respectively, after ED consumption. Another study examining seven years worth of data from an Australian poison control center found that heart palpitations/tachycardia and tremors/shaking were the two most common adverse effects of ED consumption, followed by agitation/restlessness, GI discomfort, chest pain, dizziness, paresthesia, insomnia, respiratory distress, and headache, in that order (Gunja & Brown, 2012). Another common adverse effect of caffeine consumption is anxiety, which mostly manifests after higher doses of the substance, especially in caffeine-sensitive individuals. This anxiousness is not common at lower doses, as feelings of well-being and improved mood have been shown to dominate at such levels. This adverse effect might occur because of caffeine's activation of the amygdala, which mediates both fear and anxiety (Nehlig & Boyet, 2000). Ingestion of 400 mg of caffeine was shown to produce significantly more adverse effects than 100 and 200 mg caffeine doses in one study (Astrup et al., 1990) While caffeine has a large therapeutic window, lethal doses do exist, ranging from 5-14 grams (Babu et al., 2008; Carrillo & Benitez, 2000). Because of this large window, however, the difference between the doses found in EDs and those required for lethality is prohibitively large. One would have to consume twenty-five 200 mg caffeine EDs to reach this toxic dose threshold. The FDA has, however, established an upper limit of daily caffeine consumption at 400 mg (Markey et al., 2013) – essentially only 2-3 EDs, depending on the size of the can; this amount is not associated with any adverse effects. Caffeine's pharmacokinetic properties, specifically that of its metabolism, also contribute to its toxicity. Because of its metabolism by CYP 1A2, caffeine has been known to interact with other drugs that are also metabolized by this enzyme, preventing the necessary metabolism of certain psychopharmacological substances due to concomitant caffeine metabolism (Carrillo & Benitez, 2000). This results in excessive blood plasma levels of caffeine, the drug in question, or both and can lead to drug toxicity as a result. Thus, excessive caffeine consumption is contraindicated in patients taking most psychiatric medications due to caffeine's effect on drug plasma levels (Carrillo & Benitez, 2000; Clauson et al., 2008; Ishak et al., 2012). Because of all of these adverse effects, ED companies have had to respond in the name of consumer awareness and safety. NOS and Full Throttle cans now include a warning label that states, "Too much caffeine may cause nervousness, irritability, sleeplessness, and, occasionally, rapid heartbeat," while the disclaimer on Red Bull cans reads, "Not recommended for children, pregnant or nursing women, and person sensitive to caffeine." These warning labels allude to the common adverse effects of caffeine consumption and warn ED consumers of the risks involved in drinking their product.



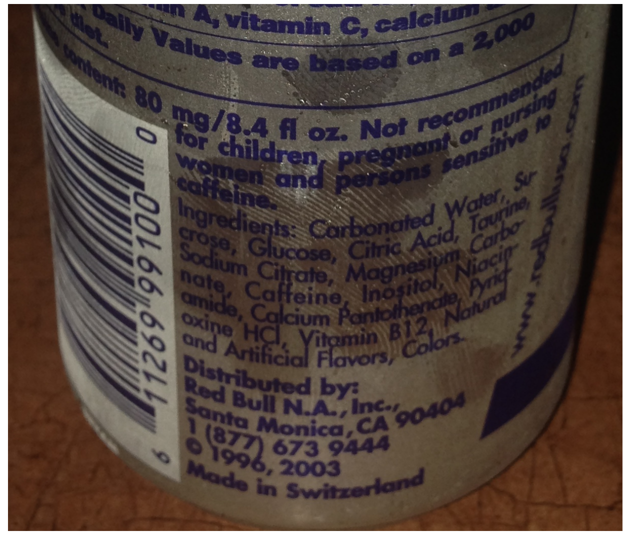


Figure 3: NOS (left) and Red Bull (right) warning labels

Guarana

Guarana, another ingredient commonly found in many EDs, is a compound derived from the seeds of a South American plant, *Paullinia cupana* (Babu et al., 2008). EDs such as Monster, NOS, Rockstar, Cocaine, and various SoBe drinks all contain guarana (Clauson et al., 2008). This herbal extract contains anywhere from 3.6-8% caffeine, as well as theobromine and theophylline, additional members of the xanthine-derivative family of which caffeine is also a member (Babu et al., 2008; Clauson et al., 2008). Because of the caffeine present in guarana, its effects are essentially those of caffeine, as caffeine is its main active ingredient. Its addition to EDs is notable, however, as it serves as an additional source of caffeine that may or may not be included in the caffeine amount listed on the can.

Glucose

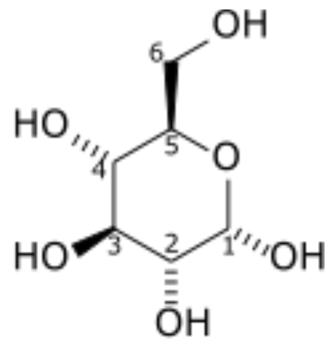


Figure 4: Chemical Structure of Glucose

Besides caffeine, sugar (in the form of glucose, sucrose, ribose, high fructose corn syrup, or a combination of these main four) is arguably the most common and necessary ingredient for any ED (Clauson et al., 2008). While the listed amount of sugar in Red Bull, for instance, is only 27 grams, other drinks like NOS and Monster contain 53 and 54 grams, respectively, due to their cans being twice as large. These latter two numbers represent 18% of one's recommended daily sugar intake, a large percent when one considers how much sugar is contained in the other beverages and food items also consumed on the average day. The high sugar levels in many EDs have been implicated in chronic illnesses such as obesity, diabetes, and heart disease and have assumedly led many ED manufacturers, such as Red Bull and Coca Cola (the maker of NOS) to now produce sugar-free versions of their respective EDs (Markey et al., 2013).

Glucose's ($C_6H_{12}O_6$ – see Figure 3 above for chemical structure) primary bodily purpose is to serve as the beginning substrate in cellular respiration – the process by which glucose is oxidized to energy in the form of ATP within the cells of our body. Because of this, glucose is the primary bodily fuel source, especially within the brain. Upon ingestion, glucose enters the bloodstream where it is distributed throughout the body and taken up by the cells for the purpose of generating ATP. The presence of glucose in the bloodstream also triggers the release of insulin, a hormone whose purpose is to regulate blood glucose levels. The consumption of EDs, with their high sugar content, triggers an insulin response as it greatly increases blood glucose levels within 30 minutes of consumption (Scholey & Kennedy, 2004; Smit et al., 2004). In a study by Scholey and Kennedy (2004), the consumption of an ED containing 37.5 grams of glucose significantly raised blood glucose levels 30 minutes after ingestion as compared to placebo (Scholey & Kennedy, 2004). Furthermore, the insulin response is negatively affected by caffeine consumption, further exacerbating the negative effects of glucose (Malinauskas et al., 2007). The mechanism for this negative interaction was not elucidated but it must surely involve caffeine interactions, direct or indirect, with insulin receptors at cell surface membranes. In addition, glucose has also been shown to increase blood plasma levels of tryptophan, an amino acid precursor of the neurotransmitter serotonin, thereby leading to increased serotonin synthesis and subsequent improvement of mood, described as “relaxing effects” (Smit et al., 2004). Glucose has also been shown to increase heart rate; the same study also showed that caffeine alone decreased heart rate and a whole ED (containing both caffeine and glucose) produced no significant change from baseline upon consumption (Scholey & Kennedy, 2004).

Taurine

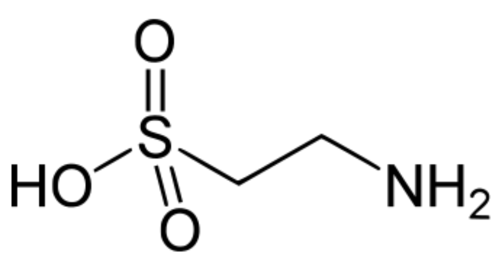


Figure 5: Chemical Structure of Taurine

Taurine, the most abundant amino acid within the cells of the human body, is another common ingredient found in EDs, including Rockstar, Monster, NOS, NOS Zero, Full Throttle, SoBe Adrenaline Rush, and SoBe No Fear, among others (Clauson et al., 2008). Though it is the most abundant amino acid in the body, taurine is a conditionally essential amino acid, meaning that the bodies of healthy adults can produce it from other amino acids but those of children and sick adults cannot – they must acquire it from their diet (Clauson et al., 2008). Thus, certain EDs high in taurine (such as Rockstar and SoBe drinks, all of which contain at least 2,000 mg of taurine) would serve as excellent sources of this conditionally essential amino acid in times of illness.

Within the body, taurine is used in the formation of taurine bile acid conjugates in the liver, which are necessary for micelle formation and fat absorption (Clauson et al., 2008). It has been reported to modulate many neurotransmitter systems, as well as act as a neurotransmitter itself (Childs & de Wit, 2008; Smit et al., 2004), thus demonstrating an effect on the CNS. More specifically, taurine exhibits positive allosteric modulatory effects on neuronal chloride channels such as $GABA_A$ and glycine channels and inhibitory effects on some cation channels such as N-methyl-D-aspartate and Ca^{+2} channels (Ferreira, de Mello, Pompeia, & de Souza-Formigoni, 2006). Taurine's effects on the heart include increased heart rate (a chronotropic effect) and increased strength of cardiac contraction (an inotropic effect), both effects also exhibited by caffeine as well (Clauson et al., 2008; Gunja & Brown, 2012). Thus, an ED containing both caffeine and taurine exerts both positive inotropic and chronotropic effects, which might result in a synergistic increase in both heart rate and strength of contraction. Taurine is also reported to have antioxidant and anti-inflammatory effects, both of which are properties that protect the body from chronic oxidative and inflammatory damage prevalent in chronic disease (Smit et al., 2004). However, sources show that 70-80% of ingested taurine is excreted within the urine inside of 24 hours after ingestion, so the effect of ingested taurine from EDs is questionable (Alford et al., 2001). The high doses of taurine used in some EDs are sufficient for the therapeutic treatment of seizures (750 mg), heart palpitations/dysrhythmias (1,000-2,000 mg), and diabetes (1,500 mg) (Clauson et al., 2008). Thus, it is possible that the addition of taurine to EDs counterbalances, to some degree, the effects of glucose on diabetes and caffeine on seizures and heart palpitations.

Ginseng

Extracts from the root of *Panax ginseng*, commonly known as Korean or Asian ginseng, are also found in EDs, including Full Throttle and Monster. As an herbal medicine, ginseng is commonly advertised as enhancing immune function, resistance to environmental stress, physical stamina, and overall well-being, though these claims by the ED industry and others have not been validated by scientific research, with only mixed results coming from the few experiments examining ginseng's physiological effects (Clauson et al., 2008). The most common therapeutic use of ginseng is in the improvement of cognitive function, concentration, and memory, with therapeutic doses ranging between 100-200 mg/day; its most common adverse effect is insomnia, a rather useful side effect if one is purposefully trying to stay awake, as is the case with most ED consumers (Clauson et al., 2008). Because of this high therapeutic dose threshold, one would have to consume multiple EDs a day to consume enough ginseng to achieve its therapeutic purposes, as its levels in EDs are typically quite low (Clauson et al., 2008). This makes ginseng's inclusion in EDs a marketing ploy, at best. That is, ED companies include the extract in their beverages to cast them as being healthy and natural and to appeal to the alternative medicine crowd. Another rare adverse effect of recurrent, high-dose ginseng administration is the onset of manic episodes, as reported in a few case histories (Clauson et al., 2008). Other studies assessing ginseng's affect on physiological and mood variables found it had no affect on any of them (Clauson et al., 2008).

After an examination of the substances contained within your average ED, it becomes clear that caffeine is the primary ingredient responsible for the psychoactive properties elicited by ED consumption. All other ingredients, except glucose, exist below their therapeutic dosages and appear to be present only as marketing ploys meant to impress unsuspecting customers and convince them that what they are purchasing might actually contain important amino acids and herbal extracts necessary for one's health. Instead, many of these additional ingredients only contribute to the unique taste of each ED. With that in mind, to understand how EDs affect the human body one must take the next step and examine how caffeine affects the human body. Fortunately, while EDs might be relatively new here in the United States, coffee is not. Thus, there exists a sufficient amount of literature regarding the effects of caffeine consumption on the human body

Chapter 3: The Cognitive/Behavioral Effects of Energy Drinks

Besides the various physiological effects previously described, EDs and their ingredients also produce certain cognitive and behavioral effects that are key to their usefulness to the consumer. It is these effects that seem to characterize ED consumption, at least to the average consumer, and are thus strongly promoted and marketed by their producers in order to increase sales. These macroscopic effects, as opposed to the often microscopic physiological effects, are what consumers notice the most. Looking back at the motivations of college students to consume EDs, three of the top four reasons were a desire to stay awake, a desire to increase energy levels, and a desire to better focus while studying for a major project or test (Malinauskas et al., 2007). All three of these motivations are reinforced by the effects of EDs, as well as the EDs industry's marketing claims promoting their products' benefits, with claims ranging from AMP Energy Boost's assertion that their drinks "energize and hydrate the body," to statements by NOS that their drinks provide "50% more focus," and Red Bull's purported ability to deliver "increased concentration and reaction speed" (Markey et al., 2013). These claims are made because the ingredients in EDs, specifically caffeine, seem to elicit certain cognitive and behavioral effects that affect a person's psychophysiological state. Recent scientific research has verified, modified, and even disproved many of these marketing claims and has shed much-needed light on the effects and consequences of ED consumption.

To measure the effect of EDs on physiological and psychological variables like alertness, reaction time, mood, memory, and attention, researchers across the board have adopted a few important tests and measures that accurately gauge these effects. Bond-Lader visual analogue scales (VAS) are commonly used as a means of self-reporting subjective feelings, such as alertness and mood. The Prolife of Mood States (POMS) is another method for participants to self-report their current subjective state, and both utilize change from baseline data to determine the significance of ED consumption on any of the dependent variables. To measure reaction time, memory, and attention, researchers use simple reaction time (SRT), two-choice reaction time (2CRT), and rapid visual information processing (RVIP) tasks. These tasks measure the time it takes the subject to respond to a particular stimulus, as determined by the type of task. For more information on each of these tests and measures, please see the Appendix.

Alertness

One of the more predominant effects of ED consumption is increased alertness. Multiple studies have shown that consumption of a whole ED or caffeine alone increases subjective ratings of alertness in participants. In a study by Haskell et al. (2005), consumption of both 75 mg and 150 mg of caffeine produced a significant increase in alertness ratings as measured by Bond-Lader visual analogue scales (VAS), coupled with decreased tiredness and mental fatigue ratings. Specifically, there was an 11 mm increase from baseline (on a 100 mm scale – see Appendix) in both treatment groups (75 mg and 150 mg) for alertness, compared to a 0.5 mm decrease in the placebo group (Haskell et al., 2005). In another article, British researchers described the results of their three studies in which EDs were repeatedly shown to improve the subjective sensation of alertness as measured by a mood questionnaire. Study 1 showed a significant improvement on the mood construct "Energetic Arousal" by consumption of an ED containing 75 mg of caffeine, 1000 mg of taurine, and 37.5 g of carbohydrates as compared to placebo; additionally, these "energizing effects" were strongest between 30 and 60 minutes after consumption (Smit et al., 2004), matching the time course at which peak plasma concentration is met. The results of Study 2 again showed that consumption of an ED (this time, without taurine) produced significant improvements in Energetic Arousal (Smit et al., 2004). In both studies, the authors described Energetic Arousal as the most strongly affected experimental construct and the most reliable indicator of caffeine's effects on the body, as ED consumption led to maintained alertness while placebo consumption led to a decrease in alertness (Smit et al., 2004).

Two studies performed by Kennedy and Scholey (2004) showed that consumption of a caffeine-containing energy drink produced decreased self-report ratings of mental fatigue in study participants. In their first study, consumption of an ED with 46 mg of caffeine produced a significant decrease in mental fatigue compared to both an ED containing 38 mg of caffeine and placebo (Kennedy & Scholey, 2004). These results show that there does appear to be a measure of dose-dependency regarding caffeine's effects on alertness, as the 38 mg of caffeine performed more similarly to the placebo without caffeine than the 46 mg caffeinated ED; in addition, these significant decreases were first seen at 30 minutes post-consumption and continued all the way to the end of the trial, at 70 minutes. In the second study, the experimental condition (utilizing an ED containing 33 mg of caffeine) produced a significant decrease in mental fatigue compared to a placebo between 30 and 50 minutes post-consumption (Kennedy & Scholey, 2004).

These results align with those of the first study, as the 33 mg condition produced effects for a shorter amount of time than the 46 mg condition, which obviously contained more caffeine. Regarding the intervals over which effects were seen, Kennedy and Scholey (2004) concluded that “the time course of improvements is consistent with the pharmacokinetic properties of caffeine, with peak plasma levels seen between 30 and 75 min following oral ingestion.” (pg. 333) It is important to note that the caffeine levels used in these three studies are well below those found in most EDs and, instead, more closely resemble those found in caffeinated soft drinks, such as Coca-Cola (which has 34 mg caffeine per 12 fl oz). Even Red Bull, with its relatively low caffeine levels, has twice as much caffeine in one can than the EDs used in the experiment. It is also important to recognize that the authors examined the effect of ED consumption on mental fatigue, what one could consider the opposite of alertness. Thus, EDs have both alerting effects and fatigue-reducing effects that can interact cooperatively to simultaneously decrease cognitive fatigue and increase alertness. So, whether you are tired or not, one does perceive increased alertness after ED consumption.

In a 2010 study examining the effects of 3 different Red Bull doses (1.8, 3.6, 5.4 mL/kg) on behavioral control, the authors found that consumption of Red Bull significantly increased subjective ratings of “stimulation” in participants that consumed either the 1.8 mL/kg (approximately 45.6 mg of caffeine) or the 5.4 mL/kg (approximately 136.7 mg of caffeine) dose compared to placebo (Howard & Marczinski, 2010). The 1.8 mL/kg dose also produced a significant increase in stimulation compared to a no-drink condition. As compared to the 1.8 and 5.4 mL/kg dose conditions, the no drink and placebo conditions actually experienced a decrease in stimulation rating, while the 3.6 mL/kg condition produced a non-significant increase (Howard & Marczinski, 2010). Thus, it was the smallest dose of Red Bull, approximating half of a normal can, which produced the greatest increase in stimulation change out of the 3 Red Bull Doses. In conjunction with stimulation, the experiment also studied the effect of Red Bull consumption on mental fatigue ratings. All 3 Red Bull doses produced significant decreases in mental fatigue compared to both the no drink and placebo conditions, with the smallest dose (1.8 mL/kg) producing the greatest decrease (Howard & Marczinski, 2010). Thus, the smallest dose of Red Bull produced both the greatest increase in stimulation and the greatest decrease in mental fatigue. As this dose corresponds to only half a can of Red Bull, results of this experiment show that the consumption of an entire can of Red Bull may not be necessary to gain the full benefits of caffeine. Additionally, the findings of this experiment reinforce the findings of the previously discussed experiment that EDs not only increase ratings of alertness, but also decrease ratings of alertness' antithesis – mental fatigue.

In a 2008 study, researchers examined the effects of a food supplement containing 200 mg of caffeine (CAF) on both mood and cognitive performance in sleep-deprived individuals (Childs & de Wit, 2008). Their results showed that use of the CAF significantly improved participants' mood relative to use of a placebo. In regards to alertness, CAF-administration significantly increased ratings of stimulant-like effects, as well as "POMS (Profile of Mood States) Vigor" (but only in participants who received the placebo in the first session and CAF in the second). From a quantitative perspective, caffeine produced a 135% change from the placebo in POMS Vigor.

Interestingly, during the sleep-deprived period before CAF-consumption (5:00 p.m. to 3:00 a.m.), participants who consumed the most caffeine on a regular basis showed the greatest decrease in POMS Vigor (Childs & de Wit, 2008). Childs and de Wit (2008) conclude that this decline in vigor might be symptomatic of ongoing caffeine withdrawal, as participants were not allowed to consume any caffeine starting at 5 p.m. and might not have consumed any since earlier that day.

In two of the earliest studies examining the effects of ED consumption, the ingestion of Red Bull produced significant improvements in subjective alertness using a Bond-Lader VAS (Alford et al., 2001; Warburton et al., 2001). In 2000, researchers from the University of the West of England published one of the foundational studies in ED research, as it has since been cited in 224 other studies, and also one of the earliest. This study, by Alford et al. (2001), found that Red Bull consumption produced a significant positive deviation of 21.9 mm from the pre-treatment baseline value for alertness, while the no drink and carbonated water conditions produced no significant deviation from baseline. A second study of Red Bull, by Warburton et al. (2001), corroborated the previous studies' findings. Though Alford et al. (2001) did not reveal the name of the ED used in their experiment, a listing of its ingredients aligns perfectly with the known ingredients of Red Bull; Warburton et al. (2001) directly identified Red Bull as the experimental drink. These researchers found that consumption of 250 mg of the ED produced a significant improvement in 3 items on a mood assessment VAS: alertness, clear-headedness, and attentiveness as compared to both a sugar-free placebo and a sugar and caffeine-containing placebo (Warburton et al., 2001). Red Bull consumption produced a significant improvement in alertness of about 12 mm compared to placebo, which produced an improvement of only about 4 mm. That amounts to three times the alertness-enhancing power as compared to placebo. Its improvement in these 3 mood factors, all sub-categories of alertness in the Bond-Lader VAS, over a placebo containing 22.5 mg of caffeine shows that the effects of caffeine are also somewhat dose-dependent (Warburton et al., 2001).

The past three and a half pages of research data and results paint a clear picture of EDs as a legitimate means to improve alertness. Only one study (Scholey & Kennedy, 2004) out of all those examining the effects of caffeine or ED consumption on alertness showed no effect. The key to understanding these results is that the variable of alertness is a subjective one, most often measured through the use of the Bond-Lader visual analogue scale (VAS) or another subjective mood assessment, such as a mood questionnaire. Though the mechanism of this subjective improvement is uncertain, caffeine's effects on the sympathetic nervous system and its activation of dopaminergic systems could be responsible for such alerting responses. Certainly, its inhibition of inhibitory adenosine receptor pathways might play a role in such stimulating responses, especially as this inhibition leads to activation of dopaminergic receptors in the striatum (Nehlig & Boyet, 2000). The sugar found in EDs might also have an effect on one's perceived levels of exertion – this is the "sugar rush" effect commonly caused by high sugar products, such as EDs. The resulting insulin spike and subsequent blood glucose crash might mitigate any effect by glucose, however. Regardless of how EDs produce this effect, the ability to generate a significant improvement in the perception of one's alertness is a benefit elicited by ED consumption and a key reason consumers purchase EDs (Malinauskas et al., 2007). In the next section, a summary of results showing that

EDs also elicit objective improvements in alertness, as measured by reaction time, will be provided to supplement the evidence showing their improvement of subjective measures of alertness.

<u>Reaction Time</u>

Alertness, as measured by self-reports and visual analogue scales, can be more quantified in terms of reaction time – the time it takes one to properly react to an experimental stimulus. Caffeine consumption was shown to produce significant improvements in different measures of reaction time in a 2004 study by Haskell et al. For simple reaction time, consumption of 75 mg of caffeine produced a significant improvement in both groups - consumers and non-consumers; the decrease in reaction time following administration of the 150 mg dose was not significant compared to placebo. Consumption of both 75 mg and 150 mg significantly decreased digit vigilance reaction time for both groups, with the 150 mg dose producing the biggest decrease in reaction time. Finally, 150 mg of caffeine produced a significant improvement in numeric working memory reaction time as compared to placebo, while the improvement produced by 75 mg was non-significant. Thus, while 75 mg was responsible for the only improvement in simple reaction time, both it and 150 mg produced significant effects on the other measures of reaction time (Haskell et al., 2005).

In a study by Kennedy and Scholey (2004) examining the effects of EDs and their constituent ingredients, both the whole drink and caffeine-only experimental groups produced a non-significant decrease in digit vigilance reaction time, while there was no effect of any of the ingredients on simple reaction time. There was, however, a trend towards decreased choice reaction time for the consumption of caffeine alone, but not for any of the other ingredients or the whole drink; consumption of the whole drink, meanwhile, produced a trend towards decreased word recognition reaction time. Besides these few results, all of which are either trends or non-significant decreases in reaction time, the authors found no effect of caffeine or ED consumption on reaction time. A 2004 study by Smit et al. found that consumption of a 250 mL ED containing 1,000 mg taurine, 75 mg caffeine, and 37.5 g carbohydrate produced a "strong overall treatment effect on reaction time" in the simple reaction time (SRT) task, one previously shown to be "highly sensitive" to the effects of caffeine on mental fatigue and alertness, as compared to water and placebo. In their conclusion, the authors declared the faster reaction time to be a consequence of the caffeine found in EDs, as opposed to the sugar, due to the results of their first two experiments (Smit et al., 2004).

The Childs and de Wit study (2005), examining the effects of a caffeine supplement, found that the CAF, containing 200 mg of caffeine, significantly improved reaction times compared to placebo in both an SRT and two-choice reaction time task (2CRT). Specifically, the median reaction time in the SRT task for placebo was 26.4 ms, compared to 12 ms for the CAF; in the 2CRT task, the median reaction time for placebo was 52.7 ms, while it was 11.2 ms for CAF (Childs & de Wit, 2008). The result is a 55% decrease in reaction time on the SRT task and a 42 ms decrease in 2CRT reaction time, all of which are attributable to the 200 mg of caffeine in the supplement (Childs & de Wit, 2008).

Different doses of Red Bull all produced significantly faster reaction times as compared to placebo in a 2010 study by Howard and Marczinski (2010). The doses used in the experiment, 1.8 mL/kg, 3.6 mL/kg, and 5.4 mL/kg, all produced a negative change in mean reaction, indicating faster reaction time, while the no drink and placebo conditions produced a positive change in mean reaction time, demonstrating that reaction times slowed down for individuals in these treatment conditions. The smallest dose (1.8 mL/kg) also produced a significant decrease in reaction time compared to the no drink condition, the only of the three Red Bull doses to do so; this fact yet again reinforces the study's conclusion that half a can of Red Bull, which is what this dose equates to, might be more effective than a whole can (Howard & Marczinski, 2010). In a 2006 study assessing the effects of Red Bull consumption on alcohol intoxication, researchers discovered that participants who drank Red Bull showed significantly improved visual reaction time compared to those who consumed alcohol plus Red Bull, who showed improved visual reaction time compared to those who consumed alcohol alone (Ferreira et al., 2006). Thus, while alcohol intoxicated the individual to the point that his/her reaction time diminished, Red Bull consumption seemingly mitigated this effect. It appears, then, that caffeine consumption not only produces positive benefits, but also seems to cancel out the negative depressant effects of alcohol, a known CNS depressant.

Alford et al.'s (2001) pivotal study on the effects of Red Bull consumption showed that Red Bull significantly improved choice reaction time as compared to placebo. In their first study, the pretreatment mean reaction time was 529.5 ms for both treatment groups. Ingestion of carbonated water produced no significant effect on choice reaction time (521.7 ms), while those who consumed Red Bull showed a significantly decreased reaction time of 433 ms. In their second study, it was again shown that Red Bull significantly improved choice reaction time compared to placebo (pretreatment mean of 559.9 ms; carbonated water = 555.5 ms; Red Bull = 528.6 ms), though the improvement was not as significant as that found in the first study. Red Bull was yet again shown to improve reaction time in Warburton et al.'s 2001 study of its cognitive effects. In this experiment, Red Bull consumption produced a significantly faster reaction time on both a rapid visual information processing (RVIP) test and a verbal reasoning test for two different experimental conditions – Red Bull vs. sugar-free placebo in participants minimally-deprived of caffeine (Study 1) and Red Bull vs. a sugar-containing, caffeine-containing (22.5 mg used only for flavor) placebo in participants who were not caffeine deprived (Study 2). The fact that Red Bull consumption produced a significant improvement in reaction time among participants in no way deprived of caffeine reinforces the notion that caffeine does, in fact, have positive effects above and beyond simple alleviation of withdrawal symptoms (Warburton et al., 2001). Furthermore, its ability to significantly improve reaction time compared to a placebo containing both sugar and low levels of caffeine indicate that is the high levels of caffeine found in EDs that are responsible for their cognitive effects, including those reaction time, and not their high sugar levels (Warburton et al., 2001).

These numerous results from multiple studies show, somewhat convincingly, that EDs do, in fact, improve reaction time. Whether it be simple reaction time, two-choice reaction time, RVIP reaction time, or verbal reasoning reaction time, consumption of an ED (most often Red Bull) produced significant improvements in this measure compared to placebo in multiple lab studies. It is important to note that all of these improvements were typically seen beginning at 30 minutes after consumption, in accordance with the body's absorption rate of caffeine. Though the improvements may be too small for the average human to notice, as they occur on the millisecond scale, they are still scientifically significant and provide further evidence that EDs have positive effects on cognition.

While the literature on why this improved reaction time occurs is sparse, it would seem that the “double-inhibitory” effects of caffeine (inhibiting an inhibitory system) on adenosine receptors would tend to increase neuronal firing and perhaps facilitate enhanced cognition. Indeed, researchers have hypothesized that caffeine’s inhibition of adenosine allows for activation (through the disinhibition) of ascending cholinergic neurons, which then increase electrical arousal within the cerebral cortex that may be responsible for caffeine’s effects on reaction time and attention (Warburton et al., 2001). A study by Nehlig and Boyet in 2000 revealed a connection between caffeine’s stimulatory effects on the body and its activation of the nigrostriatal dopaminergic pathway by doses in excess of 1.5 mg/kg; indeed, they found that this particularly dopaminergic pathway is especially sensitive to caffeine and shows not only enhanced activation, but also increased glucose utilization (Nehlig and Boyet, 2000). Regardless of how EDs produce faster reaction times, this is yet another effect of ED consumption that correlates well with consumer motivations to buy and drink these products, as faster reaction time facilitates enhanced human performance, whether it be on an exam, while studying, out with friends, or trying to stay awake and alert while driving.

Mood

The effects of ED consumption extend well beyond those of alertness and enhanced reaction time. Research shows that EDs even affect consumers’ mood, enhancing or reducing certain mood characteristics. In their 2004 study of the effects of ED ingredients on the human body, Smit et al. showed that the primary effect of the sugar found in EDs is a significant reduction in the self-reported feeling of tense as compared to placebo, followed secondarily by its tendency to reduce the jittery feeling often associated with ED consumption. This conclusion stems from data showing that a full ED significantly reduced tension compared to an ED placebo lacking carbohydrates, for which the feeling of tension actually increased over time; this reduction was not fully realized until seventy-three minutes post-consumption, suggesting these effects occur concurrently with caffeine and carbohydrate absorption. The authors concluded that ED consumption leads individuals to feel better, happier, more sociable, and, overall, in a better mood as evidenced by participants' responses to a mood questionnaire in which they scored significantly higher on these particular mood adjectives (Smit et al., 2004). The ED used in these studies contained only 75 mg of caffeine, comparable to the caffeine in Red Bull, yet also only half of what is found in other EDs, such as Monster, NOS, AMP, and Rockstar.

Consumption of a 200 mg caffeine supplement significantly increased self-report ratings of friendliness and positive mood and significantly decreased self-report ratings of depression in comparison to a placebo capsule containing no caffeine on the Profile of Mood States (POMS) 5-point scale in Child and de Wits' 2008 study of caffeine's physiological effects. These results show the effect caffeine alone has on one's mood and demonstrate the cooperative nature of mood enhancement and reduction – positive mood goes up, negative mood (depression) goes down. Whether this occurs because caffeine actually increases mood, thereby decreasing depression or vice versa is yet to be determined. The significant improvement in friendliness might also explain why many caffeine-deprived individuals become much more agreeable once they have had their caffeine fix. Interestingly, a 2004 study by Scholey and Kennedy showed no significant effects on POMS or Bond-Lader visual analogue scales used as a mood measurement. The difference, however, is that the Scholey and Kennedy study utilized a drink containing 75 mg, far below the 200 mg caffeine capsules used in the Child and de Wits study, but comparable to the levels found in a can of Red Bull or half a can of other common EDs.

Red Bull was also shown to have an effect on mood in Alford et al.'s (2001) pivotal ED study. Specifically, consumption of one can of Red Bull produced an improvement in subjective mood of 18 mm from baseline compared to carbonated water, which only produced a change of 4 mm from baseline on the Bond-Lader VAS (Alford et al., 2001). This is over 4 times the improvement in mood compared to carbonated water and demonstrates, yet again, that caffeine and sugar-containing EDs, like Red Bull, positively affect subjective mood as assessed by self-report. While self-reports are technically not the most reliable, it is telling that individuals consistently rated their own mood as higher or improved after ED ingestion as opposed to placebo. Luckily, there are also neurological reports to back up these self-reports. Using $[^{14}C]$2-deoxyglucose autoradiography on rats, French researchers discovered that caffeine, even in a low dose (1 mg/kg), activates the medial and dorsal raphe nuclei and the locus coeruleus, all structures with some command over well-being and mood (Nehlig & Boyet, 2000). This activation and subsequent increase in local cerebral glucose utilization allows these parts of the brain to increase their control over mood and would explain caffeine's ability to do so as well. Thus, the proven ability of EDs to improve mood is yet another reason for consumers to buy these beverages, as they allow consumers some form of pseudo-pharmaceutical manipulation of their own mood on a short and transient scale.

Memory/Attention

Along with mood, reaction time, and alertness, EDs have also been shown to affect memory and attention. The 2004 study by Scholey and Kennedy revealed that ED consumption significantly improved quality of memory, secondary memory, and speed of attention, while it had no significant effect on speed of memory (though there was a statistical trend towards increased speed in the ED condition), working memory, or accuracy of attention. Among the measures that ED consumption significantly improved, consumption of the other components of EDs (caffeine, glucose, and herbal fractions) produced no significant effects; this revelation led the study authors to conclude that it is the unique combination of ingredients in EDs that accounts for their "cognition enhancing properties," and not the presence of any one ingredient, even caffeine, as "neither glucose nor caffeine in isolation resulted in significant improvements of any cognitive or mood measure." (Scholey & Kennedy, 2004, p. 327). While these results conflict with other study results, this ability to produce effects not possible with consumption of only one of its constituents would seem to reinforce the "effectiveness" of EDs and discourage consumers from simply consuming one of the main ingredients, such as caffeine or glucose. Just as Kennedy and Scholey examined the effects of EDs versus those of ED ingredients, Smit and Rogers (2004) also compared the effects of the whole drink versus its ingredients and found that EDs prevented the deterioration in mood and performance over time seen in the placebo condition. Specifically, ED consumption produced both immediate and long-term improvement on RVIP performance (Smit et al., 2004).

In another study by the same authors, Kennedy and Scholey found that consumption of EDs containing well below the normal amount of caffeine found in EDs on the market today (experimental drinks containing either 38 or 46 mg caffeine) produced greater accuracy on an RVIP task, and consumption of the drink containing 46 mg of caffeine produced improved performance on the Serial 7s Subtraction task compared to placebo (Kennedy & Scholey, 2004). These two tasks comprised two-thirds of a “cognitive demand battery” that was meant to test and tax the cognitive abilities of participants in order to assess the ability of EDs to maintain cognitive performance. The study’s results led to the conclusion that EDs containing both glucose and caffeine have the ability to improve and maintain awareness during prolonged periods of high cognitive demand (Kennedy & Scholey, 2004). Without the positive effects of EDs, participants in the placebo conditions experienced decreased RVIP accuracy as time passed, as well as higher levels of mental fatigue with time (Kennedy & Scholey, 2004). The results of this study clearly show that EDs are effective in not only preventing fatigue-related declines in cognition with time, but also show some effectiveness at improving performance. Furthermore, they demonstrate that the caffeine levels found in today’s EDs (typically in excess of 80 mg and often times twice that) are above those needed to elicit scientifically significant enhancements in cognition.

In the two Red Bull studies, Red Bull consumption was shown to have conflicting effects on memory and concentration. As Alford et al. (2001) found, Red Bull produced significant improvements in memory, assessed as immediate recall, and marginally significant improvements in concentration compared to a dummy energy drink lacking caffeine and containing a low amount of sugar. Meanwhile, Warburton et al. (2001) found that Red Bull consumption had no significant effects on numerous memory measures, though it did improve attention as demonstrated through a significant increase in the mean number of detections on RVIP test. The reason for this discrepancy in memory results might be due to discrepancies in testing. In particular, the first study assessed immediate recall using two-digit numbers and oral recall, while the second used whole words and written recall. Having to remember larger chunks of information and then write them out, which could take longer than simply saying them back, might account for the insignificant effect of ED consumption on memory in the second study as it would take longer, increasing the likelihood of forgetting.

The available research literature shows that caffeine, either by itself or in an ED, does have an effect on human cognition. Multiple studies show that it can improve one's mood and feeling of alertness, as measured by either a visual analogue scale or a profile of mood states checklist. Furthermore, many of these test results should easily apply to real-world conditions, as the experiments either utilized different, though practical, doses of the same Red Bull that can be bought in convenience stores across the country or realistic, and sometimes lower, levels of caffeine that would be found in the EDs currently available for purchase. Indeed, the caffeine levels used in Kennedy & Scholey's 2004 study were well below those found in Red Bull (about half as much) or NOS and Monster (about a quarter as much); the caffeine levels used in that experiment greater approximated those found in a cup of coffee more than anything else, yet they still showed a positive effect on alertness. Caffeine was also shown to improve reaction time and attention on numerous tasks, such as the simple reaction time, two-choice reaction time, and rapid visual information processing tasks. The effects of caffeine are not limited to the mind, however; they extend to other facets of a person's life.

Chapter 4: Other Psychological Effects

Besides ED's scientifically proven effects on cognition and mood, the consumption of EDs has also been shown to have other psychological effects, due to a correlation with other drugs and problem behaviors, as well as the placebo effect that occurs upon consumption of an ED. Research has shown that these correlations do exist and have some effect on ED consumers. Understanding these correlations is important to ensure the safe consumption and use of EDs currently on the market today.

Placebo Effect

In regards to placebo effect, the taste alone of an ED has been shown to elicit certain "sensory or expectation-induced" effects on energetic arousal, hedonic tone, and overall mood constructs compared to water in Smit et al.'s 2004 study of ED components. In this study, a placebo tasting like the real ED showed immediate, but short-lasting, effects on these three experimental variables. Consumption of the placebo was shown to positively affect the feelings of "awake" and "revitalized," two of the mood components of energetic arousal, as well as the feelings of "tense" and "jittery," two of the mood components of tense arousal (Smit et al., 2004). Thus, consumers immediately felt more awake and jittery immediately after drinking the placebo drink, even though it was a chemically inert substance. The capability of the placebo to elicit significant improvements in arousal and mood immediately upon consumption demonstrates the ability of individuals to distinguish between EDs and other beverages and subconsciously assume certain benefits as a result. As these effects not only occurred with the inert drink but also before caffeine (had it even been present in the placebo) could even be fully absorbed into the bloodstream, their presence must be due to the placebo effect. Even the authors are led to conclude that the taste of an ED must have certain "stimulating oro-sensory properties" compared to water and other beverages that lead an individual to expect certain effects (Smit et al., 2004, p. 138). Furthermore, it is possible that chronic ED consumers could become conditioned to these drinks, such that the mere opening and drinking of one serves as a stimulus that immediately elicits the conditioned response – a spike in mood and energy.

This expectation of arousal is useful to ED consumers as it provides an immediate "lift" before the actual effects of caffeine consumption kick in. This placebo effect is convenient as it occurs immediately and, by the time it has dissipated, the real effects of ED ingestion have started to take effect, assuring that consumers perceive a continuous improvement in mood and cognition from the moment they put that drink down after their first sip. Due to the combination of real and placebo effects, it is also possible that EDs produce some form of operant conditioning through easily recognized positive reinforcement – that is, their benefits are easily recognized by the individual as a consequence of ED consumption, thereby increasing the likelihood of future ED consumption. Therefore, the placebo effects of ED consumption are self-reinforcing and help reassure continued consumption, accounting for one reason the ED industry has become the billion-dollar industry it is today.

Correlation with Problem Behaviors

One goal of many psychologists today is to study the interaction of different behaviors and how they contribute to or affect other behaviors. In regards to many of the common problem behaviors, ED researchers have found that these highly publicized, overly masculinized drinks often show a positive correlation with more dangerous health habits and behaviors. Indeed, a 2008 study of college students examining the correlation between EDs and certain problem behaviors showed a clear link between EDs and problem behavior syndrome, though only in white students and not in black students (Miller, 2008a). This also introduces a racial component to the relationship between ED consumption and problem behaviors, as the regular drinking of EDs showed a significant correlation with smoking, drinking, alcohol problems, and prescription drug abuse among white college students, but not among black college students (Miller, 2008a). The reason for this racial discrepancy may stem from the nature of ED companies' marketing campaigns, as most seem to focus on a target demographic that would include white young adults while precluding black young adults by advertising their drinks through extreme sports sponsorship (Red Bull, NOS, and Monster for example) and popular video games (Monster). It is in this regard that one might consider the analysis of individual ED consumption habits as a possible predictor of the likelihood of or vulnerability to more dangerous health behaviors, thereby making such an analysis a useful assessment technique of at-risk white individuals, as ED consumption showed a significant positive association with 9 out of 10 problem behaviors in the Miller study (2008). One of the most common problem behaviors commonly associated with ED use is alcohol use and abuse, which can even occur concomitantly with ED consumption. In individuals with this particular problem behavior, education on the effects of mixing alcohol with EDs is essential in order to ensure that the individual understands that just because he or she does not feel that drunk does not mean that he or she is not that drunk. This type of education is vital if DUI arrests and accidents are to be decreased, especially in college towns where the student population is especially susceptible to such drink cocktails.

Alcohol use and alcohol abuse have been shown to be twice as likely among frequent ED consumers compared to less frequent ED consumers, with a high frequency of consumption considered to be 1-2 drinks per week and anything below that falling into the low frequency category (Miller, 2008a). Another study by the same author showed that 26% of college students who responded to her 2006 Athletic Involvement Study reported mixing EDs with alcohol at least once and about half of those who did (or 13%) mixed EDs and alcohol more than once (Miller, 2008b). One in four respondents, while it might seem low, is even higher given that 39% of respondents reported consuming at least one ED in the past month (Miller, 2008b). Thus, 67% of respondents who consumed an ED in the past month also reported mixing EDs with alcohol at least once. Another study found that 54% of college-aged ED users drink alcoholic EDs, while 49% had consumed 3 or more of these mixed drinks in one setting, qualifying these individuals as alcohol abusers (Malinauskas et al., 2007). Among the general population, one study reported that only 6% of respondents had consumed alcohol and an ED in the past year, while that number rose to 21% among past-year ED users (Berger et al., 2011). This study did reveal the sociodemographic variables of the average alcoholic ED consumer. Those between the ages of 18-29 who are unemployed, single, and live in a moderate-income household are significantly more likely to consume alcoholic EDs compared to ED-only consumers (Berger et al., 2011). In addition, the authors found that middle-aged whites with a household income of $60,000 or above were more likely to consume alcohol and EDs than EDs alone (Berger et al., 2011). This date reveals a bifurcation in consumption patterns that make alcoholic EDs appeal to vastly different segments of the population. The reason for this bifurcation is as of yet unknown (Berger et al., 2011). Thus, the practice of combining alcohol and EDs appears to be fairly common among college-aged ED users, with a prevalence rate of approximately 50-67%, and less common among the general population. This difference in prevalence is significant in that college students are also more vulnerable to other problem behaviors, such as smoking and prescription drug abuse, and ED consumption might only compound such a vulnerability. Indeed, those that are "hazardous drinkers" of alcohol are also nearly 4 times more likely to mix alcohol and EDs than nonhazardous drinkers (Berger et al., 2011).

A landmark 2006 study of the effects of EDs on alcohol intoxication showed that the combination of Red Bull and vodka does reduce the subjective sensation of alcohol intoxication but has no effect on its objective measures, including blood-alcohol concentration (BAC) and visual reaction time (Ferreira et al., 2006). Regardless of the dose of vodka used, the ED and no-ED groups both had a similar BAC, with those that received the mixed drink actually having a slightly higher (though non-significant) BAC (Ferreira et al., 2006). The implications of these study results are that mixing Red Bull with one's vodka has no affect on one's BAC and will not help an individual beat a breathalyzer test even if that person does, in fact, feel less intoxicated. The combination of Red Bull and vodka also significantly reduced the occurrence of headache, weakness, dry mouth, and change in motor coordination produced by vodka alone (Ferreira et al., 2006). These decreases in the subjective sensation of alcohol intoxication are possibly due a reduction in the depressant effects of alcohol by caffeine's stimulatory effects (Ferreira et al., 2006). In addition to having no effect on BAC, the consumption of Red Bull and vodka also had no effect on visual reaction time, leading to the conclusion that mixing alcohol with an ED will not ensure the individual of the motor coordination sufficient to overcome alcohol's intoxicating effects and properly operate a vehicle (Ferreira et al., 2006).

One possible reason for the co-consumption of these two beverages is an increased "alcohol palatability" that makes it easier to consume alcohol (Ferreira et al., 2006). The sweet, sugary taste of most EDs is effective at masking the distinct, and sometimes unpleasant, taste of most liquors – a dangerous development, as this enables someone who otherwise would not be able to stomach the taste of alcohol to drink and promotes dangerous drinking habits such as rapid and/or mass consumption by making poor tasting liquors easier to ingest. Another reason for the mixing of these two drinks is the ability of EDs to mitigate the depressant effects of alcohol while maintaining the disinhibition produced by alcohol consumption and adding its own improvements in mood and arousal (Ferreira et al., 2006). This further promotes the consumption of alcohol, as it tricks the individual into thinking he/she is actually less drunk than he/she really is because the commonly noticed depressant effects of alcohol are now masked. Furthermore, the rush of energy associated with the sugar and caffeine in EDs provides the individual with energy previously not present, allowing him/her to keep drinking for a longer amount of time. This combination of taste improvement, depressant mitigation, and energy increase is a dangerous one that contributes to many cases of alcohol abuse brought on or aggravated by ED consumption. Indeed, many of the bars in this prototypical college town stock Red Bull specifically for the purpose of mixing with vodka.

Their ability to elicit an immediate placebo effect, their correlation with other problem behaviors, and their tendency to be combined with alcohol to produce a better tasting alcoholic beverage with less negative side effects all contribute to an energy drink's appeal to a uniquely suited consumer demographic. While that first cup of coffee in the morning tends to perk people up and alcoholic coffee also exists, coffee does not correlate with problem behaviors and is enjoyed by the general population, regardless of age, gender, or race. It is for these reasons that the consumer demographic for ED sales and consumption is considerably more narrow that coffee's demographic. An examination of that demographic reveals how EDs are perfectly suited to satisfy the needs of their consumers.

Chapter 5: Sociodemographic Characteristics of Energy Drink Consumers

Thus far, we have identified the major EDs on the market, their constituents, and their physiological and psychological effects. To fully understand the ED industry, one also has to understand the demographic to which these EDs are marketed and who is actually consuming them. As previously stated, the ED industry is a billion-dollar business that has exploded since the late 1990's, with the introduction of Red Bull to the American market. Since then, Red Bull has maintained and increased its dominance of the ED market, followed by other popular EDs like NOS, Monster, and AMP Energy. The success of any and all of these drinks is due to their effective ability to market to the proper demographic, which research has shown to be younger and more masculine overall, with a preference towards whites and Hispanics as compared to blacks, as well as the evolving nature of 21st century life, in which young college students and workers seem to work more and sleep less than previous generations. It is this evolving lifestyle that drives younger adults to consume these high caffeine, high sugar drinks in order to increase their energy levels and simply get through the day.

Age and Gender

A reported 30% of adolescents and anywhere from 39-51% of undergraduates have been reported to consume EDs (Babu et al., 2008; Malinauskas et al., 2007; Miller, 2008a, 2008b). The fact that at least 1 in 3 college students consume or have consumed EDs speaks to their ability to increase subjective feelings of alertness, while decreasing the perception of fatigue – a necessity for getting through any college's finals week. The majority of these ED users are male, and males are also reported to consume more EDs – 2.49 drinks vs. 1.22 drinks per month – than females (Miller, 2008b). In 2008, Miller polled 795 college students and found that 46% of males reported any ED consumption, compared to only 31% of females – a significant difference; in addition to finding that men consumed twice as many EDs than women, Miller also found that they consumed nearly twice as many alcoholic EDs (1.73 vs. .97 alcoholic EDs) and were more likely than their female counterparts to consume such beverages (Miller, 2008b). A 2011 community study showed that men are nearly 4 times more likely than women to consume EDs, while 18-29 years old are 8 times more likely than older age groups (Berger et al., 2011); this same study showed that those between the ages of 30 and 55 were 3.5 times more likely to consume EDs than those above the age of 55, indicating that ED consumption does not bottom out after one's twenties, but, instead, slowly declines. It is possible that EDs are more conducive to the on-the-go lifestyles of busy college students and working professionals, who do not have the necessary time to brew a cup of coffee or drive to Starbucks and then stand in its incredibly long line. By retirement, however, that time is available and these caffeine consumers are able to brew their own cup of coffee instead of resorting to quick and easy EDs. In addition, consumers of alcoholic EDs were also significantly more likely to be in the 18-29 year old age group, single, unemployed, and living in a household of moderate income ($30,000-60,000 annual income) than those who only drink EDs (Berger et al., 2011). This would make sense, as people in their twenties are more likely to go out, party, and consume alcohol irresponsibly than older individuals. Clearly, though, these numerous studies have shown that the majority of ED users are in their twenties, an important fact that reveals the correlation between their effects and their demographic. Simply stated, the majority of ED consumers are in their twenties because this is the age at which the effects of ED consumption are most relevant and useful to the consumer – whether it be on the go or in the classroom, workplace, or nightclub.

Race

Race is also an important sociodemographic factor, as multiple studies have reported that ED consumption is significantly higher among whites and non-black minorities compared to blacks. Miller's 2008a study found that Hispanic college students reported more frequent ED consumption than their white counterparts, yet less frequent consumption of alcoholic EDs. Miller's findings (2008a) were surprising even to herself, as the stereotypical ED consumer is typically thought of as a college-aged white male and ED marketing is typically not geared towards Hispanics. However, this finding reveals an important new consumer demographic, as Hispanics increasingly make up more and more of the U.S. population. A second study by Miller revealed the significant differences in ED consumption between white and black college students – 40% of white respondents were reported as ED users, compared to only 25% of black respondents; additionally, white ED users were reported to consume a greater (though non-significant) amount of EDs – 1.91 drinks vs. 1.47 drinks per month (Miller, 2008a). Miller's two studies reveal that Hispanics tend to consume more EDs than their white counterparts, who have a greater likelihood of consuming EDs than their black counterparts. Berger et al.'s 2011 community study of ED consumption reinforced the notion that ED consumption is higher than expected among non-black minorities, as it revealed that non-black minorities are twice as likely as whites to consumed EDs. This classification of "non-black minorities" also includes American Indians, Asian or Pacific Islanders, and Hispanics (Berger et al., 2011).

The Big Picture

These results paint a clear picture of the average ED consumer – a white or Hispanic male in his mid-twenties who is either in college or at work. An additional characteristic of this young man is what is described as the "toxic jock identity," a term invented by Miller to describe individuals with a "sport-related identity that derives as much from an ethic of risk taking and hegemonic masculinity as from any objective association with organized sports activity" that is "conducive to the kinds of health-compromising or delinquent behaviors" found by previous researchers (Miller, 2008b, p. 482). These individuals partake in and embrace risky activities as a part of their identity and the consumption of high-caffeine, high-sugar EDs can be thought of as not only one of these activities, but also as a means to facilitate other health-compromising activities. The strength of this jock identity was shown to be positively associated with the frequency of consumption for both EDs and alcoholic EDs, while conformity to masculine norms and risk-taking behavior was responsible for mediating the connection between this toxic jock identity and ED consumption (Miller, 2008b). Thus, the more a man adheres to masculine norms and partakes in risk-taking behavior, the greater his toxic jock identity is and the more he consumes both alcoholic and non-alcoholic EDs.

This toxic jock identity might be one of the contributing factors to the gender disparity in ED consumption, as women are not predisposed to follow such masculine norms and engage in poor health behaviors. It is possible that women who stay at home to raise children and maintain the household are able to work better hours and better regulate what they consume than men who are at the whims of their bosses and corporations and must adhere to strict deadlines, work long hours, and exist under stressful working conditions. This would allow them to require less caffeine and solely drink a cup of coffee in the morning. Women who work full time, however, would be the exception to this generalization – it might even be possible that they would consume more caffeine due to both work and home responsibilities. Anecdotally speaking, women who do need caffeine for work seem to consume such caffeine in the form of coffee instead of an ED, as evidenced by the popularity of Starbucks each and every morning. Indeed, the popularity of Starbucks among females might account for the relativity low popularity of EDs among this gender, as the manner is which Starbucks promotes itself is more female-friendly than many of the hyper-masculinized EDs currently on the market.

As previously mentioned, common reasons for ED consumption include counteracting insufficient sleep, increasing energy, combining with alcohol at parties, and as an aid for studying and long drives (Malinauskas et al., 2007). While the study behind these reasons was conducted solely on college students, many of these reasons can also logically apply to those beyond the college years, especially those in the workplace. EDs are most commonly consumed to prevent falling asleep and/or increase energy; most working Americans are not getting enough sleep these days, due to longer hours at work, greater work and home demands, and an ever increasing on the go lifestyle in which children must be dropped off at daycare, school, or any number of practices or rehearsals. It would make sense, then, for EDs to be a viable form of self-medication for these individuals. Thus, just like coffee, EDs are primarily used as a stimulant to increase productivity and counteract fatigue and sleep deprivation due to long hours spent working or studying. While the exact effect of ED consumption on worker/student productivity might be impossible to truly quantify, such consumption is certainly bound to counteract the effects of sleep deprivation on the average American, thereby increasing said productivity in the U.S. economy.

Chapter 6: Energy Drink Regulation

While the cause-and-effect relationship between the consumers' need for increased energy to counteract fatigue and sleep deprivation and the ability of EDs to satisfy those needs through the physiological and psychological effects of caffeine plays a major role in the popularity of today's EDs, they are not the only reason for the ED industry's rapid growth within the United States and other countries. Indeed, there are many other pharmaceutical compounds that would satisfy these needs. The difference is that those compounds are difficult to acquire, existing in either illegal (cocaine) or prescription forms (amphetamines) due to proper government regulation – regulation that, at least here in the United States, has been less enforced and less cognizant of the caffeine levels in EDs, making it easier for ED producers to make, promote, and sell their products without government regulations to slow them down. While this has been a good thing for the industry, and perhaps capitalism as a whole, it has also had it drawbacks.

Believe it or not, Red Bull, the most popular ED in the entire world, is actually banned in some countries. Due to its high caffeine content, the beverage is banned in Denmark, was banned in France until just recently, and is currently only sold in pharmacies in Norway (Kapner, 2004). This is telling, as Red Bull is most commonly bought in an 8 oz. can containing only 80 mg of caffeine, a far cry from other EDs that have at least twice as much. Why is it, then, that a drink banned for health reasons in some countries is only the tip of the iceberg of available, legal products in others? For one, it is because of the FDA. The FDA has approved caffeine as a multiple purpose generally recognized as safe (GRAS) food substance at a level of 71 mg/12 fl oz. for inclusion in food and beverages; this makes caffeine a lawful and unregulated compound (Markey et al., 2013; Somogyi, 2009). As a GRAS ingredient, companies are allowed to include caffeine in their products with only self-regulation to ensure its safety for consumers. The problem is that GRAS ingredients are determined as such not by the FDA, but by the manufacturer itself – the FDA merely supports or denies the decision, assuming there is a "reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use." (Markey et al., 2013, p. 20). While research does show that caffeine at GRAS level of 71 mg/12 fl oz. does not appear to impair health in the short-term, sparse research literature exists on the effects of chronic, high-dose caffeine consumption over time – the kind of consumption that is now possible thanks to EDs containing twice as much caffeine as a cup of coffee with additional sugar too.

This regulatory situation arises from the designation of EDs as beverages (or conventional food) as opposed to dietary supplements within the FDA's regulatory structure. This distinction is a critical one, as it allows the ED industry to operate under fewer regulations than it would if its products were considered dietary supplements. Under FDA rules and regulations, ED companies are allowed to self-determine whether their product will be marketed as one or the other (Markey et al., 2013). The implications of this ability are important, as conventional foods are less strictly regulated and monitored than dietary supplements. Listed below is a table of the key differences in regulations between the two designations, as summarized by the Congressional report.

<u>TABLE 1</u>: Key differences between the federal regulation of dietary supplements and beverages

CONVENTIONAL FOOD (BEVERAGE)	DIETARY SUPPLEMENTS
New ingredients must be approved as a food additive by the FDA, unless the ingredient is generally recognized as safe (GRAS)*	Only new ingredients not marketed in dietary supplements in the U.S. prior to October 15, 1994 require FDA preapproval. Otherwise, FDA must determine an ingredient is unsafe under conditions of use to take the product off the market
Any reporting of serious adverse events is completely voluntary	Required by law to report to the FDA any serious adverse events
Includes a "Nutrition Facts" panel on the label, with information on amount of calories, total fat, cholesterol, sodium, carbohydrates, protein, vitamin A, vitamin C, calcium and iron	Includes a "Supplement Facts" panel on the label, with information on quantities of ingredients that exceed standards or that are relevant to a product claim
Listing of ingredients in descending order of predominance is required	List the quantity of each dietary ingredient, unless the ingredient is a part of a 'proprietary blend', in which case quantities are not required
Good Manufacturing Practices (GMP) focus on ensuring safe and sanitary processing conditions	Good Manufacturing Practices (GMP) contain standards of identity to help verify that the product is what it is purported to be

* Manufacturers of a product are permitted to self-determine that an ingredient is generally recognized as safe (GRAS) without FDA affirmation

Figure 6: (Markey et al., 2013)

The ability of these companies to sell their products without being required to submit a summary of possible adverse events was a key difference early on in the life of the ED industry, as the public did not learn about the possible dangers of said drinks until news stories began to emerge detailing the numerous emergency room visits precipitated by ED consumption. Only after this public outrage did three of the popular ED manufacturers begin voluntary publishing their adverse event logs with the FDA. These logs detail the numerous emergency room visits and other adverse events related to, though not necessarily triggered by, ED consumption (FDA, 2012). Among three of the major EDs for which there was adverse event data, 5 HOUR Energy had the most reported events by far, though it is not clear whether that it due to better reporting of adverse events by the company, more adverse events per consumer, or simply more consumers to provide a larger sample size (FDA, 2012). This is most likely due to the fact that it has the highest caffeine content of all the popular EDs (and energy shots) on the market, as well as the nature in which it is consumed (Reports, 2012). Unlike other EDs, 5 HOUR Energy is a small shot which is consumed all at once. Thus, every milligram of caffeine contained within it is ingested and absorbed at the same time, instantly saturating the CYP 1A2 enzymes responsible for its metabolism and thereby allowing more of the caffeine to survive the first pass effect and enter the body's tissues through the bloodstream. These adverse events are not exclusive to the United States either. A study of Australian poison control centers found that the number of calls concerning ED consumption increased by over 500% in the six years between 2004 and 2010 (Gunja & Brown, 2012). Since the publication of these adverse event reports to the FDA, the American public has become better educated on the real-life consequences of ED consumption and over-consumption, yet adverse event reporting is still not mandatory for all EDs in the conventional food category.

As seen in Figure 5, another difference between the conventional food and dietary supplement categories is the absence of caffeine as a required disclosure on the "Nutrition Facts" label found on all conventional foods (Markey et al., 2013). Because of this, consumers were blind to the total amount of caffeine being consumed with each drink and unable to self-regulate their personal caffeine intake, as EDs in the conventional food category did not list caffeine content and EDs in the dietary supplement category masked their content by including it in a propriety blend, of which the ingredients did not have to be fully disclosed (Markey et al., 2013). Fortunately, since the publication of this influential and persuasive report by a U.S. Senator and two U.S. Representatives, it appears that most of the major ED companies have since started listing the total caffeine content of their drinks on the cans (see Figure 3 on pg. 23). This development allows for consumers to be better informed of the caffeine levels they are ingesting with each ED they purchase, allowing for better self-regulation of one's caffeine intake and a decreased probability of many of the adverse events that have been reported to the FDA. As mentioned before, the FDA limit on caffeine content is 71 mg per 12 fl oz (Markey et al., 2013). Though this rule exists, it is not enforced, nor is it airtight. In fact, it is being blatantly ignored. As shown in Table 1 (pg. 7), all of the listed EDs contain caffeine in excess of this limit. NOS contains more than twice as much caffeine in only four additional ounces. Why the FDA does not either enforce this limit or simply do away with it is subject to debate, but it is clear that its enforcement arm is not interested in going after ED manufacturers when there are "bigger fish to fry," such as the pharmaceutical companies.

This gluttony of both serving size and caffeine content has major implications on the consumer, however. The very nature of the ED lends itself to being consumed all at once, as these drinks are sold as non-resealable cans that essentially must be consumed in one sitting (Markey et al., 2013). Because of this, when one purchases a 32 oz. Monster (yes, those do exist at gas stations across America), he or she is essentially forced to drink all 108 g of sugar and all 320 mg of caffeine within a relatively short timespan; such large and relatively rapid consumption only compounds the intensity of caffeine's effects on the body, not to mention the effects of such a large sugar intake. The resulting insulin spike will be so large the individual will need all 320 mg of caffeine just to avoid the sugar crash. Thus, not only is it important that the consumer consider the caffeine content of the ED, he or she must also consider if that number is the total caffeine content or caffeine per serving; if it is simply caffeine per serving, the total amount of caffeine within the can is actually double or triple what is listed.

Conclusion

The research is clear – EDs do, in fact, work. For all of the blister and bluster surrounding their marketing – extreme sports sponsorship, edgy names and promotions, celebrity and sports superstar endorsements – these over-caffeinated soft drinks have been scientifically shown to increase one's subjective feelings of alertness and mood, as well as more objective measures of reaction time, memory, and attention (see Chapter 3). Why is it, then, that some people live and die by these drinks (and by die, I mean they feel like they are going to die if they do not get their morning fix), while others never touch them? Certainly, the very narrow demographic to which these drinks is targeted is part of the reason. After all, there are only so many twenty-something males in America (see Chapter 5). Another reason for their limited appeal is the widespread prevalence of coffee consumption – EDs with less sugar and caffeine but a bitter aftertaste. Coffee, after all, is more widely accepted amongst the general population. Your average Starbucks is significantly, both scientifically and figuratively, nicer than your average gas station convenience store, as well as a more popular location for socializing with friends. Indeed, even the stereotypical coffee drinker can be viewed in a more positive light than your average ED consumer – when one thinks of the average coffee drinker, one typically thinks of a business professional purchasing his/her morning coffee at Starbucks before going to work and returning to home later that day; the typical ED drinker, on the other hand, is a more rambunctious and masculine twenty-something male with a penchant for risk-taking behavior. These differences in perception of EDs themselves, the places where they are most commonly bought and sold, and the average ED consumer all contribute to the limited, yet strong appeal of these products. The most important reason why ED consumption is a habit for those they do appeal to and not for others might revolve around personal beliefs regarding the drinks.

Caffeine's prevalence and everyday use in our society makes this psychoactive compound almost universally accepted – from Coca-Cola to Starbucks, some of the biggest beverage brands in America include the substance in their drinks. In the face of its overwhelming presence in our society, nobody would argue against its acceptance. Yet EDs are different. They do not just contain caffeine, like Coke or coffee does; they are dominated by it, ingredient-wise. This can lead to mixed emotions and reactions to these drinks. While these high-caffeine, high-sugar drinks with aggressive ad campaigns might scare off some, others view these products as merely an extension of the already accepted caffeine beverage industry. Indeed, the perceived health threat from these drinks might seem low when we consider just how common caffeine is in our society. After all, nearly everyone consumes caffeine and the research shows that many have also consumed an ED at one point or another in their life (see Chapter 5). Clearly, the majority of people are not especially vulnerable to the effects of caffeine on health, nor are these effects perceived to have a high severity. Nobody would say that increased alertness or mood, especially at 7am in the morning or during that midday slump, is such a bad thing; at 3am, after a night of multiple Red Bull and vodkas, however, that might be a different story. Or what about at midnight as you lay in bed tossing and turning because you cannot fall asleep due to one too many EDs consumed during the day? One might feel differently then. Clearly, as with most aspects of life, moderation is the key. Consumed excessively, anything can be harmful. Indeed, many of the adverse events reported to the FDA concern excessive ED consumption to the tune of 2 or more in a relatively short time span (FDA, 2012). Though the news media has begun to publicize some of the adverse effects associated with this sort ED abuse or chronic consumption, many Americans seem to know very little about the compound they are consuming, the extent to which it is present in EDs, and the importance of its moderation in daily consumption. This lack of education poses a risk to individual health when the high levels of caffeine found in these drinks are not taken into consideration, especially in individuals sensitive to caffeine or those with hypertension, cardiovascular disease, or anxiety disorders.

One matter on which the research is not clear about is the long-term effects of chronic, high level caffeine consumption. In this literature review, the subject is not even covered due to a lack of available research. But, because of the withdrawal symptoms associated with caffeine consumption, many ED users are drawn back to their favorite brand each and every morning in an attempt to not only wake up for work or class, but also to rid themselves of the negative effects imposed by their withdrawal. This propagates a cycle in which people consume, reap the benefits, experience withdrawal, and consume again. This cycle could have long-term implications on health if it lasts many years; after all, caffeine has been shown to have some effect on heart rate and blood pressure, as well as additional adverse effects such as headaches, insomnia, and anxiety that have serious long-term implications (see Chapter 2). And, because the perceived health threat of chronic ED consumption is relatively low among the general population, such a cycle could last for many years as there would be no known benefit to stopping (except to save money, perhaps). This presents a dilemma: do the benefits of such high caffeine consumption outweigh the threats? Do the benefits of abstaining from ED consumption outweigh the withdrawal and fatigue? Future energy drink research must examine the effects of chronic ED consumption on health and whether the public is truly as educated about these products as it should be. If everyone knew just how much caffeine they were consuming on a daily basis, perhaps they would not be so quick to reach for that can of Red Bull. Then again, if everyone knew that Red Bull was scientifically proven to increase their mood, alertness, and cognition, maybe they would.

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APPENDIX

Test and Measures

1. Two choice reaction time (2CRT) task – a measure of a subject's ability to quickly distinguish between different choices; in this task, the subject is told to click the right mouse button if he/she sees two particular numbers (4 or 5) on the computer screen or the left mouse button if two other numbers (2 or 3) appear. Numbers appear at random time intervals for a total of 50 trials. Average reaction time, missed responses (stimuli to which the subject did not respond to), and accuracy (defined as the percent of correct responses). (Childs and de Wit, 2008)
2. Profile of Mood States (POMS) – a checklist of 72 mood adjectives which allows respondents to measure how they feel in regards to each adjective by ranking themselves from 0 (not at all) to 4 (extremely); the adjectives are then aggregated into 8 clusters, including anger, anxiety, confusion, depression, elation, fatigue, friendliness, and vigor (Childs & de Wit, 2008).
3. Simple reaction time (SRT) task – a measure of a subject's simple reaction time; the task consists of pressing the mouse button as quickly as possible whenever the subject sees the cue (a large asterisk) on the computer screen for a total of 100 trials. The key is that the cue appears at random times. Average reaction time, missed responses, and accuracy are the dependent measures. (Childs and de Wit, 2008; Smith et al., 2004)
4. Rapid visual information processing (RVIP) task – used to assess visual information processing speed, vigilance, and sustained attention; the task consists of presenting stimuli in the form of numerical digits on a computer screen at a

fixed rate of 100 digits/minute in a random order. Subjects are to respond by tapping the space bar whenever they see a pattern of a particular order (such as 3 odd or 3 even numbers in a row for a total of 8 patterns per minute), and their final score is measured in correct responses per minute. The maximum score is 8/minute. (Kennedy & Scholey, 2004; Smith et al., 2004)

5. Visual analogue scale (VAS) – a means of measuring subjective variables, such as feelings of alertness and fatigue; the VAS utilizes 100 mm lines with "not at all" at the 0 mm end and "extremely" at the 100 mm. Participants are asked to determine their current state by making a mark at the appropriate point on the scale; the effects of the experimental variable are measured by the change from baseline in the participants' scores. (Childs & de Wit, 2008)